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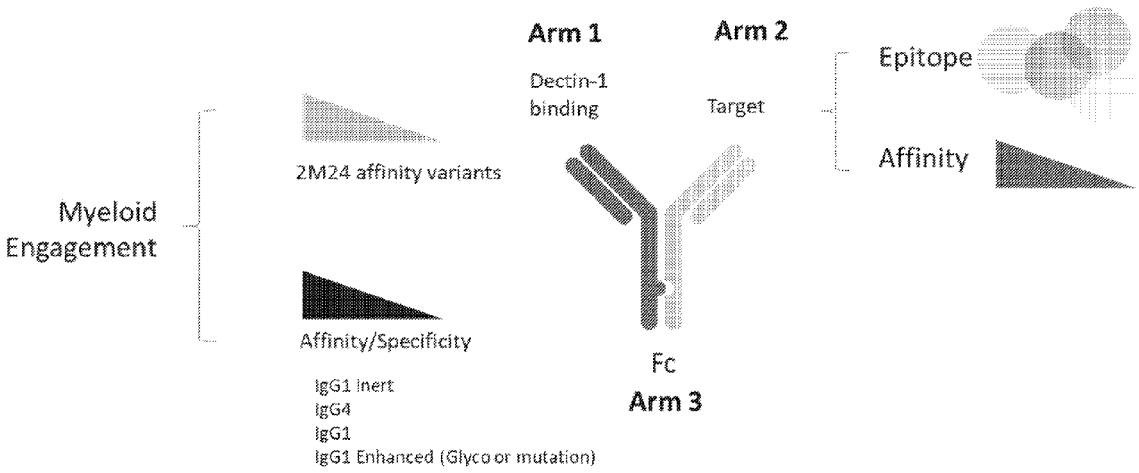


FIG. 67

(57) Abstract: The present disclosure relates to antibodies that bind human Dectin-1, multispecific (*e.g.*, bispecific) binding molecules, and methods of use and production related thereto.

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ANTI-DECTIN-1 ANTIBODIES AND METHODS OF USE THEREOF

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional Application No. 63/327,288, filed April 4, 2022, the disclosures of which are incorporated herein by reference in their entirety.

REFERENCE TO AN ELECTRONIC SEQUENCE LISTING

[0002] The contents of the electronic sequence listing (186542000640seqlist.xml; Size: 306,885 bytes; and Date of Creation: March 31, 2023) are herein incorporated by reference in their entirety.

FIELD

[0003] The present disclosure relates to antibodies that bind human Dectin-1, multispecific (*e.g.*, bispecific) binding molecules, and methods of use and production related thereto.

BACKGROUND

[0004] Phagocytosis is a major mechanism used to remove pathogens and cell debris. Professional phagocytes, such as monocytes, macrophages, dendritic cells, and granulocytes, specifically recognize and engulf host or foreign agents that are aberrant or cause disease. The engulfed material is destroyed through the endo-lysosomal pathway in the phagocytes. Moreover, dendritic cells and macrophages can present antigens to the cells of the adaptive immune system to further promote the elimination of the disease-causing agents.

[0005] Dectin-1 is a C-type lectin receptor that recognizes beta-glucans and promotes anti-fungal phagocytic activities. It is expressed on phagocytes and has been clearly shown to be sufficient for activating phagocytosis. Dectin-1 can be exploited for antibody-targeted phagocytosis and elimination of disease-causing agents.

[0006] It would be beneficial to develop targeted removal and degradation of accumulated disease-causing agents without boosting overall phagocytosis. This disclosure provides a solution for the problems and describes other advantages.

[0007] All references cited herein, including patent applications, patent publications, and scientific literature, are herein incorporated by reference in their entirety, as if each individual reference were specifically and individually indicated to be incorporated by reference.

BRIEF SUMMARY

[0008] The present disclosure relates to antibodies that bind human Dectin-1, multispecific (*e.g.*, bispecific) binding molecules, and methods of use and production related thereto. Described herein are methods of targeted phagocytosis to remove disease-causing agents, including host cells/host cell products, microbes or their products, etc., upon administration of multispecific (*e.g.*, bispecific) binding

molecules comprising a Dectin-1 binding arm and a second arm that specifically binds to the agent. The multispecific (*e.g.*, bispecific) binding molecules allow the phagocyte to engage the target agent and form a synapse between it and promote clustering of Dectin-1 on the phagocyte. This stimulates phagocytosis of the target agent and at the same time cytokine secretion via the Dectin-1/Syk/NfkB pathway by the phagocyte. Moreover, antigens from the engulfed material are presented on the surface of dendritic cells/macrophages to boost an adaptive immune response against the disease-causing agent. Overall, it is thought that the Dectin-1 agonistic, multispecific (*e.g.*, bispecific) binding molecules promote immune stimulation, targeted phagocytosis, and neo-antigen presentation/activation of the adaptive immune system to eliminate the disease-causing agent.

[0009] As such, the present disclosure describes, *inter alia*, the generation and functional characterization of an agonistic anti-human Dectin-1 antibody that exhibits high affinity binding to Dectin-1 and can promote immune stimulation, as well as variants of the antibody that are thought to modulate its binding affinity or decrease potential for immunogenicity (*i.e.*, by reverting some residues back to human germline residues and/or removing potential human T cell epitopes). Further described is the generation of bispecific antibody formats including the anti-human Dectin-1 antibodies with antibodies targeting antigens on disease-causing agents, with data supporting target engagement, immune stimulation, phagocytosis, and antigen presentation.

[0010] In some embodiments, provided herein is an antibody or antigen-binding fragment thereof that binds to human Dectin-1, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises the amino acid sequence QVQLVQSGAEVKKPGASVKVSCKSSGYTFTX$_1$YYIHWVRQAPGQGLEWMGWINPNSGX$_2$TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCAX$_3$X$_4$X$_5$X$_6$X$_7$X$_8$X$_9$X$_{10}$X$_{11}$X$_{12}$WGQGTLVTVSS, wherein X$_1$ is D, A, or G; wherein X$_2$ is D, A, or G; wherein X$_3$ is R, A, or G; wherein X$_4$ is N, A, or G; wherein X$_5$ is S, A, or G; wherein X$_6$ is A or G; wherein X$_7$ is S, A, or G; wherein X$_8$ is Y, A, or G; wherein X$_9$ is S, A, or G; wherein X$_{10}$ is F, A, or G; wherein X$_{11}$ is A or G; and wherein X$_{12}$ is Y, A, or G (SEQ ID NO:63); wherein the VL domain comprises the amino acid sequence DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPSRFSGSGSGTDFTLTVSSLQPEDFATYYCX$_1$X$_2$AX$_3$X$_4$X$_5$X$_6$X$_7$X$_8$FGPGTKVDIE, wherein X$_1$ is Q, A, or G; X$_2$ is Q, A, or G; X$_3$ is F, Y, A, or G; wherein X$_4$ is S, A, or G; wherein X$_5$ is F, A, or G; wherein X$_6$ is P, A, or G; wherein X$_7$ is F, A, or G; and wherein X$_8$ is T, A, or G (SEQ ID NO:65). In some embodiments, the antibody does not comprise a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3), a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the VH domain comprises 1, 2 or fewer, 3 or fewer, 4 or fewer, or 5 or

fewer substitutions as compared to the amino acid sequence of SEQ ID NO:62; and/or wherein the VL domain comprises 1, 2 or fewer, 3 or fewer, 4 or fewer, or 5 or fewer substitutions as compared to the amino acid sequence of SEQ ID NO:64. In some embodiments, the antibody or fragment binds to human Dectin-1 expressed on the surface of a cell with an EC50 of less than 2nM; is capable of binding human or cynomolgus Dectin-1; and/or does not compete with a native ligand of human Dectin-1.

[0011] In some embodiments, provided herein is an antibody or antigen-binding fragment thereof that binds to human Dectin-1, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises: a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1) or AYYI (SEQ ID NO: 16); a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2) or WINPNSGATNYAQKFQG (SEQ ID NO: 19); and a CDR-H3 comprising an amino acid sequence selected from the group consisting of NSGSYSFGY (SEQ ID NO: 3), ASGSYSFGY (SEQ ID NO: 22), NSGSASFGY (SEQ ID NO: 24), NAGSYSFGY (SEQ ID NO: 27), NSASYSFGY (SEQ ID NO: 29), NSGAYSFGY (SEQ ID NO: 31), NSGSYAFGY (SEQ ID NO: 33), NSGSYSAGY (SEQ ID NO: 35), NSGSYSFAY (SEQ ID NO: 37), and NSGSYSFGA (SEQ ID NO: 39); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4); a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising an amino acid sequence selected from the group consisting of QQAYSFPFT (SEQ ID NO: 6), QQAASFPFT (SEQ ID NO: 41), QQAFSFPFT (SEQ ID NO: 42), AQAYSFPFT (SEQ ID NO: 43), QAAYSFPFT (SEQ ID NO: 44), QQAYAFPFT (SEQ ID NO: 45), QQAYSAPFT (SEQ ID NO: 46), QQAYSFAFT (SEQ ID NO: 47), QQAYSFPAT (SEQ ID NO: 48), and QQAYSFPFA (SEQ ID NO: 49). In some embodiments, the antibody does not comprise a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3), a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence AYYI (SEQ ID NO: 16), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGATNYAQKFQG (SEQ ID NO: 19), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence

WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence ASGSYSFGY (SEQ ID NO: 22). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSASFGY (SEQ ID NO: 24). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NAGSYSFGY (SEQ ID NO: 27). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSASYSFGY (SEQ ID NO: 29). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGAYSFGY (SEQ ID NO: 31). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYAFGY (SEQ ID NO: 33). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSAGY (SEQ ID NO: 35). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSFAY (SEQ ID NO: 37). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSFGA (SEQ ID NO: 39). In some embodiments, the VH domain further comprises a FR1 comprising an amino acid sequence selected from the group consisting of QVQLVQSGAEVKKPGASVKVSCKSSGYTFT (SEQ ID NO:50) and QVQLVQSGAEVKKPGASVKVSCKASGYTFT (SEQ ID NO:51); a FR2 comprising the amino acid sequence HWVRQAPGQGLEWMG (SEQ ID NO:52); a FR3 comprising an amino acid sequence selected from the group consisting of RITMTRDTSISTAYLELSRLRSDDTAVFYCAR (SEQ ID NO:53) and RVTMTRDTSISTAYMELSRLRSDDTAVYYCAR (SEQ ID NO:54); and a FR4 comprising the amino acid sequence WGQGTLVTVSS (SEQ ID NO:55). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the

amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAASFPFT (SEQ ID NO: 41). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAFSFPFT (SEQ ID NO: 42). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence AQAYSFPFT (SEQ ID NO: 43). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QAAYSFPFT (SEQ ID NO: 44). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYAFPFT (SEQ ID NO: 45). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSAPFT (SEQ ID NO: 46). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFAFT (SEQ ID NO: 47). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPAT (SEQ ID NO: 48). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFA (SEQ ID NO: 49). In some embodiments, the VL domain further comprises a FR1 comprising the amino acid sequence DIQMTQSPSSVSASVGDRVTITC (SEQ ID NO:56); a FR2 comprising an amino acid sequence selected from the group consisting of WYQQKPGKAPKLLIF (SEQ ID NO:57) and WYQQKPGKAPKLLIY (SEQ ID NO:58); a FR3 comprising an amino acid sequence selected from the group consisting of GVPSRFSGSGSGTDFTLTVSSLQPEDFATYYC (SEQ ID NO:59) and GVPSRFSGSGSGTDFTLTISSLQPEDFATYYC (SEQ ID NO:60); and a FR4 comprising the amino acid sequence FGPGTKVDIE (SEQ ID NO:61).

[0012] In some embodiments, provided herein is an antibody or antigen-binding fragment thereof that binds to human Dectin-1, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises: a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7) or GYTFTAYY (SEQ ID NO:17); a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8) or INPNSGAT (SEQ ID NO:

20); and a CDR-H3 comprising an amino acid sequence selected from the group consisting of ARNSGSYSFGY (SEQ ID NO: 9), ARASGSYSFGY (SEQ ID NO: 23), ARNSGSASFGY (SEQ ID NO: 25), AANSGSYSFGY (SEQ ID NO: 26), ARNAGSYSFGY (SEQ ID NO: 28), ARNSASYSFGY (SEQ ID NO: 30), ARNSGAYSFGY (SEQ ID NO: 32), ARNSGSYAFGY (SEQ ID NO: 34), ARNSGSYSAGY (SEQ ID NO: 36), ARNSGSYSFAY (SEQ ID NO: 38), and ARNSGSYSFGA (SEQ ID NO: 40); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10); a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising an amino acid sequence selected from the group consisting of QQAYSFPFT (SEQ ID NO: 12), QQAASFPFT (SEQ ID NO: 41), QQAFSFPFT (SEQ ID NO: 42), AQAYSFPFT (SEQ ID NO: 43), QAAYSFPFT (SEQ ID NO: 44), QQAYAFPFT (SEQ ID NO: 45), QQAYSAPFT (SEQ ID NO: 46), QQAYSFAFT (SEQ ID NO: 47), QQAYSFPAT (SEQ ID NO: 48), and QQAYSFPFA (SEQ ID NO: 49). In some embodiments, the antibody does not comprise a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), a CDR-H3 comprising the amino acid sequence ARNSGSYSFGY (SEQ ID NO: 9), a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 12). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARNSGSYSFGY (SEQ ID NO: 9). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTAYY (SEQ ID NO:17), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARNSGSYSFGY (SEQ ID NO: 9). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGAT (SEQ ID NO: 20), and a CDR-H3 comprising the amino acid sequence ARNSGSYSFGY (SEQ ID NO: 9). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARASGSYSFGY (SEQ ID NO: 23). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARNSGSASFGY (SEQ ID NO: 25). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence AANSGSYSFGY (SEQ ID NO: 26). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence

ARNAGSYSFGY (SEQ ID NO: 28). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARNSASYSFGY (SEQ ID NO: 30). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARNSGAYSFGY (SEQ ID NO: 32). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARNSGSYAFGY (SEQ ID NO: 34). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARNSGSYSAGY (SEQ ID NO: 36). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARNSGSYSFAY (SEQ ID NO: 38). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARNSGSYSFGA (SEQ ID NO: 40). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 12). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence QQAASFPFT (SEQ ID NO: 41). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence QQAFSFPFT (SEQ ID NO: 42). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence AQAYSFPFT (SEQ ID NO: 43). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence QAAYSFPFT (SEQ ID NO: 44). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence QQAYAFPFT (SEQ ID NO: 45). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3

comprising the amino acid sequence QQAYSAPFT (SEQ ID NO: 46). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence QQAYSFAFT (SEQ ID NO: 47). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence QQAYSFPAT (SEQ ID NO: 48). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence QQAYSFPFA (SEQ ID NO: 49).

[0013] In some embodiments, provided herein is an antibody or antigen-binding fragment thereof that binds to human Dectin-1, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises: a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13) or GYTFTAY (SEQ ID NO:18); a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14) or NPNSGA (SEQ ID NO: 21); and a CDR-H3 comprising an amino acid sequence selected from the group consisting of NSGSYSFGY (SEQ ID NO: 15), ASGSYSFGY (SEQ ID NO: 22), NSGSASFGY (SEQ ID NO: 24), NAGSYSFGY (SEQ ID NO: 27), NSASYSFGY (SEQ ID NO: 29), NSGAYSFGY (SEQ ID NO: 31), NSGSYAFGY (SEQ ID NO: 33), NSGSYSAGY (SEQ ID NO: 35), NSGSYSFAY (SEQ ID NO: 37), and NSGSYSFGA (SEQ ID NO: 39); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4); a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising an amino acid sequence selected from the group consisting of QQAYSFPFT (SEQ ID NO: 6), QQAASFPFT (SEQ ID NO: 41), QQAFSFPFT (SEQ ID NO: 42), AQAYSFPFT (SEQ ID NO: 43), QAAYSFPFT (SEQ ID NO: 44), QQAYAFPFT (SEQ ID NO: 45), QQAYSAPFT (SEQ ID NO: 46), QQAYSFAFT (SEQ ID NO: 47), QQAYSFPAT (SEQ ID NO: 48), and QQAYSFPFA (SEQ ID NO: 49). In some embodiments, the antibody does not comprise a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 15), a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 15). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTAY (SEQ ID NO:18), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 15). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid

sequence NPNSGA (SEQ ID NO: 21), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 15). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence ASGSYSFGY (SEQ ID NO: 22). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence NAGSYSFGY (SEQ ID NO: 27). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence NSASYSFGY (SEQ ID NO: 29). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence NSGAYSFGY (SEQ ID NO: 31). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence NSGSYAFGY (SEQ ID NO: 33). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence NSGSYSAGY (SEQ ID NO: 35). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence NSGSYSFAY (SEQ ID NO: 37). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence NSGSYSFGA (SEQ ID NO: 39). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAASFPFT (SEQ ID NO: 41). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAFSFPFT (SEQ ID NO: 42). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence AQAYSFPFT (SEQ ID NO: 43). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence

RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QAAYSFPFT (SEQ ID NO: 44). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYAFPFT (SEQ ID NO: 45). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSAPFT (SEQ ID NO: 46). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFAFT (SEQ ID NO: 47). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPAT (SEQ ID NO: 48). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFA (SEQ ID NO: 49).

[0014] In some embodiments, the VH domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos:62 and 82-93. In some embodiments, In some embodiments according to any of the embodiments described herein, the VL domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos: 64 and 94-102. In some embodiments, the VH domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos:62 and 82-93 and/or the VL domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos: 64 and 94-102. In some embodiments, the antibody does not comprise a VH domain comprising the amino acid sequence of SEQ ID NO:62 and a VL domain comprising the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain comprises

the amino acid sequence of SEQ ID NO:62, and the VL domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:82, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:82, and the VL domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:83, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:83, and the VL domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:84, and the VL domain

comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:84, and the VL domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:85, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:85, and the VL domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:86, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:86, and the VL domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain comprises the amino acid sequence of SEQ ID NO:95. In some

embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:87, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:87, and the VL domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:88, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:88, and the VL domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID

NO: 88, and the VL domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:89, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:89, and the VL domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:90, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:90, and the VL domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain comprises the amino acid sequence of

SEQ ID NO:100. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:91, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:91, and the VL domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:92, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:92, and the VL domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain comprises

the amino acid sequence of SEQ ID NO:93, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:93, and the VL domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain comprises the amino acid sequence of SEQ ID NO:102.

[0015] In some embodiments, provided herein is an antibody or antigen-binding fragment thereof that binds to human Dectin-1, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises the amino acid sequence QVQLVQSGAEVKKPGASVKVSCKX$_1$SGYTFTX$_2$YYX$_3$HWVRQAPGQGLEWMGWINPNSGX$_4$TNYAQKFQGRX$_5$TMTRDTSISTAYX$_6$ELSRLRSDDTAVX$_7$YCARNSGSYSFGYWGQGTLVTVSS; wherein X_1 is S or A; wherein X_2 is D or G; wherein X_3 is I or M; wherein X_4 is D or G; wherein X_5 is I or V; wherein X_6 is L or M; and wherein X_7 is F or Y (SEQ ID NO:80); and wherein the VL domain comprises the amino acid sequence DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIX$_1$X$_2$ASSLQSGVPSRFSGSGSGTDFTLTX$_3$SSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE; wherein X_1 is F or Y; wherein X_2 is G or A; and wherein X_3 is V or I (SEQ ID NO:81). In some embodiments, the antibody does not comprise a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3), a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6).

[0016] In some embodiments, provided herein is an antibody or antigen-binding fragment thereof that binds to human Dectin-1, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises: a CDR-H1 comprising an amino acid sequence selected from the group consisting of DYYI (SEQ ID NO: 1), DYYM

(SEQ ID NO: 66), and GYYM (SEQ ID NO: 67); a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2) or WINPNSGGTNYAQKFQG (SEQ ID NO: 70); and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4); a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5) or AASSLQS (SEQ ID NO: 73), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the antibody does not comprise a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3), a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence DYYM (SEQ ID NO: 66), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYYM (SEQ ID NO: 67), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence DYYM (SEQ ID NO: 66), a CDR-H2 comprising the amino acid sequence WINPNSGGTNYAQKFQG (SEQ ID NO: 70), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYYM (SEQ ID NO: 67), a CDR-H2 comprising the amino acid sequence WINPNSGGTNYAQKFQG (SEQ ID NO: 70), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3). In some embodiments, the VH domain further comprises a FR1 comprising an amino acid sequence selected from the group consisting of QVQLVQSGAEVKKPGASVKVSCKSSGYTFT (SEQ ID NO:50) and QVQLVQSGAEVKKPGASVKVSCKASGYTFT (SEQ ID NO:76); a FR2 comprising the amino acid sequence HWVRQAPGQGLEWMG (SEQ ID NO:52); a FR3 comprising an amino acid sequence selected from the group consisting of RITMTRDTSISTAYLELSRLRSDDTAVFYCAR (SEQ ID NO:53) and RVTMTRDTSISTAYMELSRLRSDDTAVYYCAR (SEQ ID NO:77); and a FR4 comprising the amino acid sequence WGQGTLVTVSS (SEQ ID NO:55). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the VL domain comprises a CDR-

L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence AASSLQS (SEQ ID NO: 73), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the VL domain further comprises a FR1 comprising the amino acid sequence DIQMTQSPSSVSASVGDRVTITC (SEQ ID NO:56); a FR2 comprising an amino acid sequence selected from the group consisting of WYQQKPGKAPKLLIF (SEQ ID NO:57) and WYQQKPGKAPKLLIY (SEQ ID NO:78); a FR3 comprising an amino acid sequence selected from the group consisting of GVPSRFSGSGSGTDFTLTVSSLQPEDFATYYC (SEQ ID NO:59) and GVPSRFSGSGSGTDFTLTISSLQPEDFATYYC (SEQ ID NO:79); and a FR4 comprising the amino acid sequence FGPGTKVDIE (SEQ ID NO:61). In some embodiments, the VH domain comprises: a CDR-H1 comprising the amino acid sequence of DYYM (SEQ ID NO: 199), a CDR-H2 comprising the amino acid sequence of WINPNEGDTNYAQKFEG (SEQ ID NO: 200), and a CDR-H3 comprising the amino acid sequence of NTGAYSFGY (SEQ ID NO: 204); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASDLQS (SEQ ID NO: 206), and a CDR-L3 comprising the amino acid sequence of QQAYGFPFT (SEQ ID NO: 207). In some embodiments, the VH domain comprises: a CDR-H1 comprising the amino acid sequence of DYYM (SEQ ID NO: 199), a CDR-H2 comprising the amino acid sequence of WINPNEGDTNYAQKFQE (SEQ ID NO: 201), and a CDR-H3 comprising the amino acid sequence of NTGAYSFGY (SEQ ID NO: 204); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASDLQS (SEQ ID NO: 206), and a CDR-L3 comprising the amino acid sequence of HQAYSFPFT (SEQ ID NO: 208).

[0017] In some embodiments, provided herein is an antibody or antigen-binding fragment thereof that binds to human Dectin-1, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises: a CDR-H1 comprising an amino acid sequence selected from the group consisting of GYTFTDYY (SEQ ID NO:7), and GYTFTGYY (SEQ ID NO:68); a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8) or INPNSGGT (SEQ ID NO:71); and a CDR-H3 comprising the amino acid sequence ARNSGSYSFGY (SEQ ID NO: 9); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10); a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11) or AAS (SEQ ID NO: 74), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 12). In some embodiments, the antibody does not comprise a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), a CDR-H3 comprising the amino acid sequence ARNSGSYSFGY (SEQ ID NO: 9), a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 12). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-

H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARNSGSYSFGY (SEQ ID NO: 9). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTGYY (SEQ ID NO:68), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARNSGSYSFGY (SEQ ID NO: 9). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGGT (SEQ ID NO:71), and a CDR-H3 comprising the amino acid sequence ARNSGSYSFGY (SEQ ID NO: 9). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTGYY (SEQ ID NO:68), a CDR-H2 comprising the amino acid sequence INPNSGGT (SEQ ID NO:71), and a CDR-H3 comprising the amino acid sequence ARNSGSYSFGY (SEQ ID NO: 9). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 12). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence AAS (SEQ ID NO: 74), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 12). In some embodiments, the VH domain comprises: a CDR-H1 comprising the amino acid sequence of GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence of INPNEGDT (SEQ ID NO: 202), and a CDR-H3 comprising the amino acid sequence of ARNTGAYSFGY (SEQ ID NO: 205); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence of QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence of GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence of QQAYGFPFT (SEQ ID NO: 207). In some embodiments, the VH domain comprises: a CDR-H1 comprising the amino acid sequence of GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence of INPNEGDT (SEQ ID NO: 202), and a CDR-H3 comprising the amino acid sequence of ARNTGAYSFGY (SEQ ID NO: 205); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence of QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence of GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence of HQAYSFPFT (SEQ ID NO: 208).

[0018] In some embodiments, provided herein is an antibody or antigen-binding fragment thereof that binds to human Dectin-1, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises: a CDR-H1 comprising an amino acid sequence selected from the group consisting of GYTFTDY (SEQ ID NO:13), and GYTFTGY (SEQ ID NO:69); a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14) or NPNSGG (SEQ ID NO: 72); and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 15); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4); a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5) or AASSLQS (SEQ ID NO: 75), and a CDR-L3 comprising the amino acid

sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the antibody does not comprise a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 15), a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 15). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTGY (SEQ ID NO:69), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 15). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGG (SEQ ID NO: 72), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 15). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTGY (SEQ ID NO:69), a CDR-H2 comprising the amino acid sequence NPNSGG (SEQ ID NO: 72), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 15). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence AASSLQS (SEQ ID NO: 75), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the VH domain comprises: a CDR-H1 comprising the amino acid sequence of GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence of NPNEGD (SEQ ID NO: 203), and a CDR-H3 comprising the amino acid sequence of NTGAYSFGY (SEQ ID NO: 204); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASDLQS (SEQ ID NO: 206), and a CDR-L3 comprising the amino acid sequence of QQAYGFPFT (SEQ ID NO: 207). In some embodiments, the VH domain comprises: a CDR-H1 comprising the amino acid sequence of GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence of NPNEGD (SEQ ID NO: 203), and a CDR-H3 comprising the amino acid sequence of NTGAYSFGY (SEQ ID NO: 204); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASDLQS (SEQ ID NO: 206), and a CDR-L3 comprising the amino acid sequence of HQAYSFPFT (SEQ ID NO: 208).

[0019] In some embodiments, the VH domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos: 62 and 103-109. In some embodiments, the VL domain comprises an

amino acid sequence selected from the group consisting of SEQ ID Nos:64 and 110-113. In some embodiments, the VH domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos: 62 and 103-109 and/or the VL domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos:64 and 110-113. In some embodiments, the antibody does not comprise a VH domain comprising the amino acid sequence of SEQ ID NO:62 and a VL domain comprising the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 62, and the VL domain comprises the amino acid sequence of SEQ ID NO:110. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 62, and the VL domain comprises the amino acid sequence of SEQ ID NO:111. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 62, and the VL domain comprises the amino acid sequence of SEQ ID NO:112. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 62, and the VL domain comprises the amino acid sequence of SEQ ID NO:113. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 103, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 103, and the VL domain comprises the amino acid sequence of SEQ ID NO:110. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 103, and the VL domain comprises the amino acid sequence of SEQ ID NO:111. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 103, and the VL domain comprises the amino acid sequence of SEQ ID NO:112. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 103, and the VL domain comprises the amino acid sequence of SEQ ID NO:113. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 104, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 104, and the VL domain comprises the amino acid sequence of SEQ ID NO:110. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 104, and the VL domain comprises the amino acid sequence of SEQ ID NO:111. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 104, and the VL domain comprises the amino acid sequence of SEQ ID NO:112. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 104, and the VL domain comprises the amino acid sequence of SEQ ID NO:113. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 105, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 105, and the VL domain comprises the amino acid sequence of SEQ ID NO:110. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 105, and the VL domain comprises the amino acid sequence of SEQ ID NO:111. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 105, and the VL domain comprises the amino acid sequence of SEQ ID NO:112. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 105, and the VL domain comprises the amino acid sequence of SEQ ID NO:113. In some

embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 106, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 106, and the VL domain comprises the amino acid sequence of SEQ ID NO:110. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 106, and the VL domain comprises the amino acid sequence of SEQ ID NO:111. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 106, and the VL domain comprises the amino acid sequence of SEQ ID NO:112. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 106, and the VL domain comprises the amino acid sequence of SEQ ID NO:113. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 107, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 107, and the VL domain comprises the amino acid sequence of SEQ ID NO:110. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 107, and the VL domain comprises the amino acid sequence of SEQ ID NO:111. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 107, and the VL domain comprises the amino acid sequence of SEQ ID NO:112. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 107, and the VL domain comprises the amino acid sequence of SEQ ID NO:113. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 108, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 108, and the VL domain comprises the amino acid sequence of SEQ ID NO:110. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 108, and the VL domain comprises the amino acid sequence of SEQ ID NO:111. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 108, and the VL domain comprises the amino acid sequence of SEQ ID NO:112. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 108, and the VL domain comprises the amino acid sequence of SEQ ID NO:113. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 109, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 109, and the VL domain comprises the amino acid sequence of SEQ ID NO:110. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 109, and the VL domain comprises the amino acid sequence of SEQ ID NO:111. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 109, and the VL domain comprises the amino acid sequence of SEQ ID NO:112. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 109, and the VL domain comprises the amino acid sequence of SEQ ID NO:11.

[0020] In some embodiments, the VH domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos: 62, 103-109, 194-196, 209, 211, 213, 215, and 220. In some embodiments, the VL domain comprises an amino acid sequence selected from the group consisting of

SEQ ID Nos:64, 110-113, 197, 198, 210, 212, 214, 216, and 221. In some embodiments, the VH domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos: 62, 103-109, 194-196, 209, 211, 213, 215, and 220, and the VL domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos:64, 110-113, 197, 198, 210, 212, 214, 216, and 221. In some embodiments, the VH domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos: 62, 194-196, 209, 211, 213, 215, and 220. In some embodiments, the VL domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos:64, 197, 198, 210, 212, 214, 216, and 221. In some embodiments, the VH domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos: 62, 194-196, 209, 211, 213, 215, and 220, and the VL domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos:64, 197, 198, 210, 212, 214, 216, and 221. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 209, and the VL domain comprises the amino acid sequence of SEQ ID NO:210. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 211, and the VL domain comprises the amino acid sequence of SEQ ID NO:212. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 213, and the VL domain comprises the amino acid sequence of SEQ ID NO:214. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 220, and the VL domain comprises the amino acid sequence of SEQ ID NO:221. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 195, and the VL domain comprises the amino acid sequence of SEQ ID NO:64.

[0021] In some embodiments, provided herein is an antibody or antigen-binding fragment thereof that binds to human Dectin-1, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises: a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1) or DYYM (SEQ ID NO: 199); a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), WINPNEGDTNYAQKFEG (SEQ ID NO: 200), or WINPNEGDTNYAQKFQE (SEQ ID NO: 201); and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3), NSGSASFGY (SEQ ID NO: 187), NSGSYSAGY (SEQ ID NO: 190), or NTGAYSFGY (SEQ ID NO: 204); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4); a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5) or GASDLQS (SEQ ID NO: 206), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6), QAAYSFPFT (SEQ ID NO: 192), QQAYSAPFT (SEQ ID NO: 193), QQAYGFPFT (SEQ ID NO: 207), or HQAYSFPFT (SEQ ID NO: 208); wherein the antibody does not comprise a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3), a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the VH

domain comprises: a CDR-H1 comprising the amino acid sequence of DYYM (SEQ ID NO: 199), a CDR-H2 comprising the amino acid sequence of WINPNEGDTNYAQKFEG (SEQ ID NO: 200), and a CDR-H3 comprising the amino acid sequence of NTGAYSFGY (SEQ ID NO: 204), and the VL domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASDLQS (SEQ ID NO: 206), and a CDR-L3 comprising the amino acid sequence of QQAYGFPFT (SEQ ID NO: 207). In some embodiments, the VH domain comprises: a CDR-H1 comprising the amino acid sequence of DYYM (SEQ ID NO: 199), a CDR-H2 comprising the amino acid sequence of WINPNEGDTNYAQKFQE (SEQ ID NO: 201), and a CDR-H3 comprising the amino acid sequence of NTGAYSFGY (SEQ ID NO: 204), and the VL domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASDLQS (SEQ ID NO: 206), and a CDR-L3 comprising the amino acid sequence of HQAYSFPFT (SEQ ID NO: 208). In some embodiments, the VH domain comprises: a CDR-H1 comprising the amino acid sequence of DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence of WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence of NSGSASFGY (SEQ ID NO: 187), and the VL domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence of QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the VH domain comprises: a CDR-H1 comprising the amino acid sequence of DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence of WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence of NSGSYSAGY (SEQ ID NO: 190), and the VL domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence of QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the VH domain comprises: a CDR-H1 comprising the amino acid sequence of DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence of WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence of NSGSYSFGY (SEQ ID NO: 3), and the VL domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence of QAAYSFPFT (SEQ ID NO: 192). In some embodiments, the VH domain comprises: a CDR-H1 comprising the amino acid sequence of DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence of WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence of NSGSYSFGY (SEQ ID NO: 3), and the VL domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence of QQAYSAPFT (SEQ ID NO: 193). In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 209, and the VL domain comprises the amino acid sequence of SEQ ID

NO:210. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 211, and the VL domain comprises the amino acid sequence of SEQ ID NO:212. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 220, and the VL domain comprises the amino acid sequence of SEQ ID NO:221. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 194, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 196, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 62, and the VL domain comprises the amino acid sequence of SEQ ID NO:197. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 62, and the VL domain comprises the amino acid sequence of SEQ ID NO:198.

[0022] In some embodiments, the antibody or fragment is a human, humanized, or chimeric antibody or fragment. In some embodiments, the antibody or fragment binds to human Dectin-1 expressed on the surface of a macrophage, monocyte, dendritic cell, and/or granulocyte. In some embodiments, the antigen-binding antibody fragment is a Fab, Fab', F(ab')2, Fv, Fab'-SH, F(ab')2, single chain antibody, nanobody, or scFv fragment. In some embodiments, the antibody further comprises an Fc region. In some embodiments, the Fc region is a human IgG Fc region. In some embodiments, the Fc region is a human IgG1 or human IgG4 Fc region. In some embodiments, the Fc region is a human IgG1 Fc region comprising S239D and I332E substitutions, according to EU numbering. In some embodiments, the Fc region is a human IgG1 Fc region comprising S239D, A330L, and I332E substitutions, according to EU numbering. In some embodiments, the Fc region is a human IgG1 Fc region comprising G236A, S239D, A330L, and I332E substitutions, according to EU numbering. In some embodiments, the Fc region is a human IgG4 Fc region comprising an S228P substitution, according to EU numbering. In some embodiments, the antibody or fragment is a multispecific antibody or fragment. In some embodiments, the antibody or fragment is a bispecific antibody, fragment, or diabody comprising a first antigen binding domain comprising the VH and VL domains that bind to human Dectin-1 and a second antigen binding domain that binds to a target of interest or comprising a first antigen binding domain that binds to a target of interest and a second antigen binding domain comprising the VH and VL domains that bind to human Dectin-1. In some embodiments, the bispecific antibody comprises a first antibody arm comprising a single chain variable fragment (scFv) comprising the VH and VL domains that bind to human Dectin-1 and a first Fc region, and a second antibody arm comprising an antibody heavy chain that comprises the VH domain of the second antigen binding domain in association with an antibody light chain that comprises the VL domain of the second antigen binding domain and a second Fc region connected to the VH domain of the second antigen binding domain. In some embodiments, the VH domain that binds to human Dectin-1 comprises the amino acid sequence of SEQ ID NO:220, and wherein the VL domain that binds to human Dectin-1 comprises the amino acid sequence of SEQ ID NO:221. In some embodiments, the scFv comprises the amino acid sequence of SEQ ID NO:222. In some embodiments, the first antibody arm comprises the amino acid sequence of SEQ ID NO:224 or 225. In some embodiments, the second

antigen-binding domain binds to CD20 and comprises a VH domain comprising the sequence of SEQ ID NO:129 and a VL domain comprising the sequence of SEQ ID NO:130. In some embodiments, the second antigen-binding domain binds to Trop-2 and comprises a VH domain comprising the sequence of SEQ ID NO:139 and a VL domain comprising the sequence of SEQ ID NO:140. In some embodiments, the second antigen-binding domain binds to light chain amyloid and comprises a VH domain comprising the sequence of SEQ ID NO:143 and a VL domain comprising the sequence of SEQ ID NO:144. In some embodiments, the first Fc region comprises one or more knob-forming mutations, and the second Fc region comprises one or more cognate hole-forming mutations, or wherein the second Fc region comprises one or more knob-forming mutations, and the first Fc region comprises one or more cognate hole-forming mutations. In some embodiments, the first Fc region comprises a T366W substitution, and the second Fc region comprises T366S, L368A, and Y407V substitutions, according to EU numbering. In some embodiments, the first antibody arm comprises a first linker between the VH and VL domains, and a second linker between the VL domain and the first Fc region. In some embodiments, the first linker comprises one or more repeats of the sequence GGGGS (SEQ ID NO:115). In some embodiments, the first linker comprises the sequence GGGGSGGGGSGGGGS (SEQ ID NO:116) or GGGGSGGGGSGGGGSGGGGS (SEQ ID NO:117). In some embodiments, the second linker comprises the sequence EPKRSDKTHTCPPC (SEQ ID NO:118) or SATHTCPPC (SEQ ID NO:119). In some embodiments, the bispecific antibody comprises a first IgG antibody comprising the first antigen binding domain covalently linked to a second IgG antibody comprising the second antigen binding domain. In some embodiments, the bispecific antibody comprises a first antibody arm comprising a first antibody heavy chain that comprises the VH domain of the first antigen binding domain and a first Fc region and a second antibody arm comprising a second antibody heavy chain that comprises the VH domain of the second antigen binding domain and a second Fc region, wherein the first Fc region comprises one or more knob-forming mutations, and the second Fc region comprises one or more cognate hole-forming mutations. In some embodiments, the first Fc region comprises a T366W substitution, and the second Fc region comprises T366S, L368A, and Y407V substitutions, according to EU numbering. In some embodiments, the bispecific antibody comprises a first antibody arm comprising a first antibody heavy chain that comprises the VH domain of the first antigen binding domain and a first Fc region and a second antibody arm comprising a second antibody heavy chain that comprises the VH domain of the second antigen binding domain and a second Fc region, wherein the first Fc region comprises one or more hole-forming mutations, and the second Fc region comprises one or more cognate knob-forming mutations. In some embodiments, the first Fc region comprises T366S, L368A, and Y407V substitutions, and the second Fc region comprises a T366W substitution, according to EU numbering. In some embodiments, the bispecific antibody comprises two antibody heavy chains and two antibody light chains, wherein the VH domain of the first antibody heavy chain forms an antigen binding domain with the VL domain of the first antibody light chain that binds human Dectin-1, wherein the VH domain of the second antibody heavy chain forms an antigen binding domain with the VL domain of the second antibody light chain that

binds a target of interest; wherein the VH domain of the first antibody heavy chain comprises the amino acid sequence of SEQ ID NO:209, and wherein the VL domain of the first antibody light chain comprises the amino acid sequence of SEQ ID NO:210. In some embodiments, the bispecific antibody comprises two antibody heavy chains and two antibody light chains, wherein the VH domain of the first antibody heavy chain forms an antigen binding domain with the VL domain of the first antibody light chain that binds human Dectin-1, wherein the VH domain of the second antibody heavy chain forms an antigen binding domain with the VL domain of the second antibody light chain that binds a target of interest; wherein the VH domain of the first antibody heavy chain comprises the amino acid sequence of SEQ ID NO:220, and wherein the VL domain of the first antibody light chain comprises the amino acid sequence of SEQ ID NO:221. In some embodiments, the first antibody heavy chain comprises a C→S substitution at position 5, according to IMGT hinge numbering, and wherein the first antibody light chain comprises a C→S substitution at the terminal residue of the light chain constant domain. In some embodiments, the first antibody heavy chain comprises the amino acid sequence of SEQ ID NO:219, and wherein the first antibody light chain comprises the amino acid sequence of SEQ ID NO:223. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 213, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:214. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 195, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the bispecific antibody comprises a first IgG antibody comprising the first antigen binding domain coupled to biotin or an avidin-binding derivative thereof, and a second IgG antibody comprising the second antigen binding domain coupled to avidin, streptavidin, neutravidin, or a biotin-binding derivative thereof, wherein the biotin or avidin-binding derivative thereof is bound to the avidin, streptavidin, neutravidin, or biotin-binding derivative thereof. In some embodiments, the bispecific antibody comprises a first IgG antibody comprising the first antigen binding domain coupled to avidin, streptavidin, neutravidin, or a biotin-binding derivative thereof, and a second IgG antibody comprising the second antigen binding domain coupled to biotin or an avidin-binding derivative thereof, wherein the biotin or avidin-binding derivative thereof is bound to the avidin, streptavidin, neutravidin, or biotin-binding derivative thereof.

[0023] In some embodiments, provided herein is a multispecific (*e.g.*, bispecific) binding molecule that comprises a first antibody or antigen-binding fragment thereof comprising a first antigen binding domain, wherein the first antigen binding domain binds to human Dectin-1; and a second antibody or antigen-binding fragment thereof comprising a second antigen binding domain, wherein the second antigen binding domain binds to a target of interest; wherein the first antigen binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain of the first antigen binding domain comprises: a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1) or DYYM (SEQ ID NO: 199); a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), WINPNEGDTNYAQKFEG (SEQ ID NO: 200), or WINPNEGDTNYAQKFQE (SEQ ID NO: 201); and a CDR-H3 comprising the amino acid sequence

NSGSYSFGY (SEQ ID NO: 3), NSGSASFGY (SEQ ID NO: 187), NSGSYSAGY (SEQ ID NO: 190), or NTGAYSFGY (SEQ ID NO: 204); and wherein the VL domain of the first antigen binding domain comprises: a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4); a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5) or GASDLQS (SEQ ID NO: 206), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6), QAAYSFPFT (SEQ ID NO: 192), QQAYSAPFT (SEQ ID NO: 193), QQAYGFPFT (SEQ ID NO: 207), or HQAYSFPFT (SEQ ID NO: 208); wherein the multispecific binding molecule does not comprise a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3), a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the VH domain of the first antigen binding domain comprises: a CDR-H1 comprising the amino acid sequence of DYYM (SEQ ID NO: 199), a CDR-H2 comprising the amino acid sequence of WINPNEGDTNYAQKFEG (SEQ ID NO: 200), and a CDR-H3 comprising the amino acid sequence of NTGAYSFGY (SEQ ID NO: 204), and the VL domain of the first antigen binding domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASDLQS (SEQ ID NO: 206), and a CDR-L3 comprising the amino acid sequence of QQAYGFPFT (SEQ ID NO: 207). In some embodiments, the VH domain of the first antigen binding domain comprises: a CDR-H1 comprising the amino acid sequence of DYYM (SEQ ID NO: 199), a CDR-H2 comprising the amino acid sequence of WINPNEGDTNYAQKFQE (SEQ ID NO: 201), and a CDR-H3 comprising the amino acid sequence of NTGAYSFGY (SEQ ID NO: 204), and the VL domain of the first antigen binding domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASDLQS (SEQ ID NO: 206), and a CDR-L3 comprising the amino acid sequence of HQAYSFPFT (SEQ ID NO: 208). In some embodiments, the VH domain of the first antigen binding domain comprises: a CDR-H1 comprising the amino acid sequence of DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence of WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence of NSGSASFGY (SEQ ID NO: 187), and the VL domain of the first antigen binding domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence of QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the VH domain of the first antigen binding domain comprises: a CDR-H1 comprising the amino acid sequence of DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence of WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence of NSGSYSAGY (SEQ ID NO: 190), and the VL domain of the first antigen binding domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2

comprising the amino acid sequence of GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence of QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the VH domain of the first antigen binding domain comprises: a CDR-H1 comprising the amino acid sequence of DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence of WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence of NSGSYSFGY (SEQ ID NO: 3), and the VL domain of the first antigen binding domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence of QAAYSFPFT (SEQ ID NO: 192). In some embodiments, the VH domain of the first antigen binding domain comprises: a CDR-H1 comprising the amino acid sequence of DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence of WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence of NSGSYSFGY (SEQ ID NO: 3), and the VL domain of the first antigen binding domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence of QQAYSAPFT (SEQ ID NO: 193). In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 209, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:210. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 211, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:212. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 220, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:221. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 194, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 196, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 62, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:197. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 62, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:198. In some embodiments, the VH domain of the first antibody arm comprises the amino acid sequence of SEQ ID NO:220, and wherein the VL domain of the first antibody arm comprises the amino acid sequence of SEQ ID NO:221.

[0024] In some embodiments, provided herein is a multispecific (*e.g.*, bispecific) binding molecule that comprises a first antibody arm comprising a single chain variable fragment (scFv) comprising VH and VL domains of the present disclosure that bind to human Dectin-1 and a first Fc region, and a second antibody

arm comprising an antibody heavy chain that comprises a VH domain in association with an antibody light chain that comprises a VL domain and a second Fc region connected to the VH domain, wherein the VH and VL domains of the second antibody arm form an antigen binding domain that binds to a target of interest (*e.g.*, other than human Dectin-1). In some embodiments, the scFv of the first antibody arm comprises a VH domain that comprises the amino acid sequence of SEQ ID NO: 209, and a VL domain that comprises the amino acid sequence of SEQ ID NO:210. In some embodiments, the scFv of the first antibody arm comprises a VH domain that comprises the amino acid sequence of SEQ ID NO: 213, and a VL domain that comprises the amino acid sequence of SEQ ID NO:214. In some embodiments, the scFv of the first antibody arm comprises a VH domain that comprises the amino acid sequence of SEQ ID NO: 220, and a VL domain that comprises the amino acid sequence of SEQ ID NO:221. In some embodiments, the scFv of the first antibody arm comprises the amino acid sequence QVQLVQSGAEVKKPGASVKVSCKASGYTFTDYYMHWVRQAPGQGLEWMGWINPNEG DTNYAQKFEGRITMTRDTSISTAYMELSRLRSDDTAVYYCARNTGAYSFGYWGCGTLV TVSSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSVSASVGDRVTITCRASQGISSWLAW YQQKPGKCPKLLIYGASDLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQAYGFPF TFGPGTKVDIKEPK (SEQ ID NO:222). In some embodiments, the first antibody arm comprises the amino acid sequence QVQLVQSGAEVKKPGASVKVSCKASGYTFTDYYMHWVRQAPGQGLEWMGWINPNEG DTNYAQKFEGRITMTRDTSISTAYMELSRLRSDDTAVYYCARNTGAYSFGYWGCGTLV TVSSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSVSASVGDRVTITCRASQGISSWLAW YQQKPGKCPKLLIYGASDLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQAYGFPF TFGPGTKVDIKEPKRSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCK VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPG (SEQ ID NO:224) or QVQLVQSGAEVKKPGASVKVSCKASGYTFTDYYMHWVRQAPGQGLEWMGWINPNEG DTNYAQKFEGRITMTRDTSISTAYMELSRLRSDDTAVYYCARNTGAYSFGYWGCGTLV TVSSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSVSASVGDRVTITCRASQGISSWLAW YQQKPGKCPKLLIYGASDLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQAYGFPF TFGPGTKVDIKEPKRSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCK VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK (SEQ ID NO:225).

[0025] In some embodiments, the first VH domain comprises the amino acid sequence of SEQ ID NO: 213, and the first VL domain comprises the amino acid sequence of SEQ ID NO:214. In some embodiments, the first VH domain comprises the amino acid sequence of SEQ ID NO: 220, and the first VL domain comprises the amino acid sequence of SEQ ID NO:221. In some embodiments, the antibody heavy chain of the first antibody arm has a C→S amino acid substitution at position 5, according to IMGT hinge numbering; position 220, according to EU index; or position 233, according to Kabat numbering. In some embodiments, the antibody heavy chain of the first antibody arm comprises the sequence ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSSDKTHTCPPCPAPELLGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSR EEMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG (SEQ ID NO:219). In some embodiments, the antibody light chain of the first antibody arm has a C→S at the terminal residue of the light chain constant domain (*e.g.*, CK domain). In some embodiments, the antibody light chain of the first antibody arm comprises the sequence RADAAPTVSIFPPSSEQLTSGGASVVCFLNNFYPKDINVKWKIDGSERQNGVLNSWTDQ DSKDSTYSMSSTLTLTKDEYERHNSYTCEATHKTSTSPIVKSFNRNES (SEQ ID NO:223). In some embodiments, the first VH domain comprises the amino acid sequence of SEQ ID NO: 213; the first VL domain comprises the amino acid sequence of SEQ ID NO:214; the antibody heavy chain of the first antibody arm has a C→S amino acid substitution at position 5, according to IMGT hinge numbering; position 220, according to EU index; or position 233, according to Kabat numbering; and the antibody light chain of the first antibody arm has a C→S at the terminal residue of the light chain constant domain (*e.g.*, CK domain). In some embodiments, the first VH domain comprises the amino acid sequence of SEQ ID NO: 220; the first VL domain comprises the amino acid sequence of SEQ ID NO:221; the antibody heavy chain of the first antibody arm has a C→S amino acid substitution at position 5, according to IMGT hinge numbering; position 220, according to EU index; or position 233, according to Kabat numbering; and the antibody light chain of the first antibody arm has a C→S at the terminal residue of the light chain constant domain (*e.g.*, CK domain). In some embodiments, the first VH domain comprises the amino acid sequence of SEQ ID NO: 213; the first VL domain comprises the amino acid sequence of SEQ ID NO:214; the antibody heavy chain of the first antibody arm comprises the sequence of SEQ ID NO:219; and the antibody light chain of the first antibody arm comprises the sequence of SEQ ID NO:223. In some embodiments, the first VH domain comprises the amino acid sequence of SEQ ID NO: 220; the first VL domain comprises the amino acid sequence of SEQ ID NO:221; the antibody heavy chain of the first antibody arm comprises the sequence of SEQ ID NO:219; and the antibody light chain of the first antibody arm comprises the sequence of SEQ ID NO:223.

[0026] In some embodiments, the target of interest is a disease-causing agent. In some embodiments, the disease-causing agent is a bacterial cell, fungal cell, virus, senescent cell, tumor cell, protein aggregate (*e.g.*, amyloid beta, or lambda or kappa light chain amyloids), LDL particle, mast cell, eosinophil, ILC2 cell, or inflammatory immune cell. In some embodiments, the target of interest is an antigen expressed on the surface of the bacterial cell, fungal cell, senescent cell, tumor cell, mast cell, eosinophil, ILC2 cell, or inflammatory immune cell. In some embodiments, the target of interest is a surface antigen of the virus. In some embodiments, the target of interest is an antigen expressed on the surface of a cancer cell. In some embodiments, the target of interest is CD70, HER2, DLL3, NECTIN-4, TROP-2, Mesothelin, LIV-1, C-MET, FOLR1, CD20, CCR8, CD33, or EGFR. In some embodiments, the target of interest is CD20; the second antigen-binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; and the VH domain of the second antigen-binding domain comprises the sequence QVQLQQPGAELVKPGASVKMSCKASGYTFTSYNMHWVKQTPGRGLEWIGAIYPGNGDTSYNQ KFKGKATLTADKSSSTAYMQLSSLTSEDSAVYYCARSTYYGGDWYFNVWGAGTTVTVSA (SEQ ID NO:129) and/or the VL domain of the second antigen-binding domain comprises the sequence QIVLSQSPAILSASPGEKVTMTCRASSSVSYIHWFQQKPGSSPKPWIYATSNLASGVPVRFSGSGS GTSYSLTISRVEAEDAATYYCQQWTSNPPTFGGGTKLEIK (SEQ ID NO:130). In some embodiments, the antibody comprises two antibody heavy chains, and wherein each of the antibody heavy chains comprises an amino acid substitution at one or more of positions 234, 235, and 237, according to EU numbering. In some embodiments, each of the antibody heavy chains comprises L234A, L235E, and G237A substitutions, according to EU numbering. In some embodiments, the antibody comprises two antibody heavy chains, and wherein only one of the antibody heavy chains comprises H435R and Y436F substitutions, according to EU numbering. In some embodiments, the antibody comprises two arms, and only one of the antibody arms comprises a heavy chain comprising F126C and C220V substitutions and a light chain comprising S121C and C214V substitutions, according to EU numbering. In some embodiments, the bispecific antibody comprises a first and a second antibody heavy chain, wherein the VH domain of the first antibody heavy chain forms an antigen binding domain with the VL domain of the first antibody light chain, wherein the VH domain of the second antibody heavy chain forms an antigen binding domain with the VL domain of the second antibody light chain, wherein the first antibody heavy chain comprises F126C, C220V, and T366W substitutions, wherein the first antibody light chain comprises S121C and C214V substitutions, and wherein the second antibody heavy chain comprises T366S, L368A, Y407V, H435R, and Y436F substitutions, according to EU numbering. In some embodiments, the first and second antibody heavy chains further comprise L234A, L235E, and G237A substitutions, according to EU numbering.

[0027] In some embodiments, the first and second antibody heavy chains comprise human IgG1 Fc domains. In some embodiments, the antibody comprises a first and a second antibody heavy chain, wherein at least one or two of the first and second antibody heavy chains is/are non-fucosylated or comprise(s) reduced fucosylation. In some embodiments, the antibody may be produced in a cell line

having an alpha1,6-fucosyltransferase (Fut8) or alpha-1,3-mannosyl-glycoprotein 2-beta-N-acetylglucosaminyltranferase (MGAT1) knockout. In some embodiments, the antibody may be produced in a cell line overexpressing β1,4-N-acetylglucosaminyltransferase III (GnT-III). In further embodiments, the cell line additionally overexpresses Golgi μ-mannosidase II (ManII). In some embodiments, the antibody may be produced in a cell line treated with an inhibitor of mannosidase I, *e.g.*, kifunensine.

[0028] In some embodiments, provided herein is a multispecific binding molecule, comprising: (a) a first antibody or antigen-binding fragment thereof comprising a first antigen-binding domain, wherein the first antigen-binding domain binds to human Dectin-1; and (b) a second antibody or antigen-binding fragment thereof comprising a second antigen-binding domain, wherein the second antigen binding domain binds to a target of interest; wherein the first antigen-binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain of the first antigen-binding domain comprises the amino acid sequence QVQLVQSGAEVKKPGASVKVSCKSSGYTFTX$_1$YYIHWVRQAPGQGLEWMGWINPNSGX$_2$TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCAX$_3$X$_4$X$_5$X$_6$X$_7$X$_8$X$_9$X$_{10}$X$_{11}$X$_{12}$WGQGTLVTVSS, wherein X$_1$ is D, A, or G; wherein X$_2$ is D, A, or G; wherein X$_3$ is R, A, or G; wherein X$_4$ is N, A, or G; wherein X$_5$ is S, A, or G; wherein X$_6$ is A or G; wherein X$_7$ is S, A, or G; wherein X$_8$ is Y, A, or G; wherein X$_9$ is S, A, or G; wherein X$_{10}$ is F, A, or G; wherein X$_{11}$ is A or G; and wherein X$_{12}$ is Y, A, or G (SEQ ID NO:63); and wherein the VL domain of the first antigen-binding domain comprises the amino acid sequence DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPSRFSGSGSGTDFTLTVSSLQPEDFATYYCX$_1$X$_2$AX$_3$X$_4$X$_5$X$_6$X$_7$X$_8$FGPGTKVDIE, wherein X$_1$ is Q, A, or G; X$_2$ is Q, A, or G; X$_3$ is F, Y, A, or G; wherein X$_4$ is S, A, or G; wherein X$_5$ is F, A, or G; wherein X$_6$ is P, A, or G; wherein X$_7$ is F, A, or G; and wherein X$_8$ is T, A, or G (SEQ ID NO:65). In some embodiments, the first antigen-binding domain does not comprise a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3), a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the VH domain of the first antigen-binding domain comprises 1, 2 or fewer, 3 or fewer, 4 or fewer, or 5 or fewer substitutions as compared to the amino acid sequence of SEQ ID NO:62; and/or wherein the VL domain of the first antigen-binding domain comprises 1, 2 or fewer, 3 or fewer, 4 or fewer, or 5 or fewer substitutions as compared to the amino acid sequence of SEQ ID NO:64. In some embodiments, the first antigen-binding domain binds to human Dectin-1 expressed on the surface of a cell with an EC50 of less than 2nM; is capable of binding human or cynomolgus Dectin-1; and/or does not compete with a native ligand of human Dectin-1.

[0029] In some embodiments, provided herein is a multispecific binding molecule, comprising: (a) a first antibody or antigen-binding fragment thereof comprising a first antigen-binding domain, wherein the

first antigen-binding domain binds to human Dectin-1; and (b) a second antibody or antigen-binding fragment thereof comprising a second antigen-binding domain, wherein the second antigen binding domain binds to a target of interest; wherein the first antigen-binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain of the first antigen-binding domain comprises: a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1) or AYYI (SEQ ID NO: 16); a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2) or WINPNSGATNYAQKFQG (SEQ ID NO: 19); and a CDR-H3 comprising an amino acid sequence selected from the group consisting of NSGSYSFGY (SEQ ID NO: 3), ASGSYSFGY (SEQ ID NO: 22), NSGSASFGY (SEQ ID NO: 24), NAGSYSFGY (SEQ ID NO: 27), NSASYSFGY (SEQ ID NO: 29), NSGAYSFGY (SEQ ID NO: 31), NSGSYAFGY (SEQ ID NO: 33), NSGSYSAGY (SEQ ID NO: 35), NSGSYSFAY (SEQ ID NO: 37), and NSGSYSFGA (SEQ ID NO: 39); and wherein the VL domain of the first antigen-binding domain comprises: a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4); a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising an amino acid sequence selected from the group consisting of QQAYSFPFT (SEQ ID NO: 6), QQAASFPFT (SEQ ID NO: 41), QQAFSFPFT (SEQ ID NO: 42), AQAYSFPFT (SEQ ID NO: 43), QAAYSFPFT (SEQ ID NO: 44), QQAYAFPFT (SEQ ID NO: 45), QQAYSAPFT (SEQ ID NO: 46), QQAYSFAFT (SEQ ID NO: 47), QQAYSFPAT (SEQ ID NO: 48), and QQAYSFPFA (SEQ ID NO: 49). In some embodiments, the first antigen-binding domain does not comprise a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3), a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6).

[0030] In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence AYYI (SEQ ID NO: 16), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGATNYAQKFQG (SEQ ID NO: 19), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence ASGSYSFGY (SEQ ID NO: 22). In some

embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSASFGY (SEQ ID NO: 24). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NAGSYSFGY (SEQ ID NO: 27). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSASYSFGY (SEQ ID NO: 29). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGAYSFGY (SEQ ID NO: 31). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYAFGY (SEQ ID NO: 33). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSAGY (SEQ ID NO: 35). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSFAY (SEQ ID NO: 37). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSFGA (SEQ ID NO: 39). In some embodiments, the VH domain of the first antigen binding domain further comprises a FR1 comprising an amino acid sequence selected from the group consisting of QVQLVQSGAEVKKPGASVKVSCKSSGYTFT (SEQ ID NO:50) and QVQLVQSGAEVKKPGASVKVSCKASGYTFT (SEQ ID NO:51); a FR2 comprising the amino acid sequence HWVRQAPGQGLEWMG (SEQ ID NO:52); a FR3 comprising an amino acid sequence selected from the group consisting of RITMTRDTSISTAYLELSRLRSDDTAVFYCAR (SEQ ID NO:53) and RVTMTRDTSISTAYMELSRLRSDDTAVYYCAR (SEQ ID NO:54); and a FR4 comprising the amino acid sequence WGQGTLVTVSS (SEQ ID NO:55). In some embodiments, the VL domain of the first antigen binding domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the

VL domain of the first antigen binding domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAASFPFT (SEQ ID NO: 41). In some embodiments, the VL domain of the first antigen binding domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAFSFPFT (SEQ ID NO: 42). In some embodiments, the VL domain of the first antigen binding domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence AQAYSFPFT (SEQ ID NO: 43). In some embodiments, the VL domain of the first antigen binding domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QAAYSFPFT (SEQ ID NO: 44). In some embodiments, the VL domain of the first antigen binding domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYAFPFT (SEQ ID NO: 45). In some embodiments, the VL domain of the first antigen binding domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSAPFT (SEQ ID NO: 46). In some embodiments, the VL domain of the first antigen binding domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFAFT (SEQ ID NO: 47). In some embodiments, the VL domain of the first antigen binding domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPAT (SEQ ID NO: 48). In some embodiments, the VL domain of the first antigen binding domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFA (SEQ ID NO: 49). In some embodiments, the VL domain of the first antigen binding domain further comprises a FR1 comprising the amino acid sequence DIQMTQSPSSVSASVGDRVTITC (SEQ ID NO:56); a FR2 comprising an amino acid sequence selected from the group consisting of WYQQKPGKAPKLLIF (SEQ ID NO:57) and WYQQKPGKAPKLLIY (SEQ ID NO:58); a FR3 comprising an amino acid sequence selected from the group consisting of GVPSRFSGSGSGTDFTLTVSSLQPEDFATYYC (SEQ ID NO:59) and GVPSRFSGSGSGTDFTLTISSLQPEDFATYYC (SEQ ID NO:60); and a FR4 comprising the amino acid sequence FGPGTKVDIE (SEQ ID NO:61).

[0031] In some embodiments, provided herein is a multispecific binding molecule, comprising: (a) a first antibody or antigen binding fragment thereof comprising a first antigen binding domain, wherein the first antigen binding domain binds to human Dectin-1; and (b) a second antibody or antigen-binding fragment thereof comprising a second antigen-binding domain, wherein the second antigen binding domain binds to a target of interest; wherein the first antigen binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain of the first antigen binding domain comprises: a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7) or GYTFTAYY (SEQ ID NO:17); a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8) or INPNSGAT (SEQ ID NO: 20); and a CDR-H3 comprising an amino acid sequence selected from the group consisting of ARNSGSYSFGY (SEQ ID NO: 9), ARASGSYSFGY (SEQ ID NO: 23), ARNSGSASFGY (SEQ ID NO: 25), AANSGSYSFGY (SEQ ID NO: 26), ARNAGSYSFGY (SEQ ID NO: 28), ARNSASYSFGY (SEQ ID NO: 30), ARNSGAYSFGY (SEQ ID NO: 32), ARNSGSYAFGY (SEQ ID NO: 34), ARNSGSYSAGY (SEQ ID NO: 36), ARNSGSYSFAY (SEQ ID NO: 38), and ARNSGSYSFGA (SEQ ID NO: 40); and wherein the VL domain of the first antigen binding domain comprises: a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10); a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising an amino acid sequence selected from the group consisting of QQAYSFPFT (SEQ ID NO: 12), QQAASFPFT (SEQ ID NO: 41), QQAFSFPFT (SEQ ID NO: 42), AQAYSFPFT (SEQ ID NO: 43), QAAYSFPFT (SEQ ID NO: 44), QQAYAFPFT (SEQ ID NO: 45), QQAYSAPFT (SEQ ID NO: 46), QQAYSFAFT (SEQ ID NO: 47), QQAYSFPAT (SEQ ID NO: 48), and QQAYSFPFA (SEQ ID NO: 49). In some embodiments, the first antigen binding domain does not comprise a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), a CDR-H3 comprising the amino acid sequence ARNSGSYSFGY (SEQ ID NO: 9), a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 12). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARNSGSYSFGY (SEQ ID NO: 9). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence GYTFTAYY (SEQ ID NO:17), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARNSGSYSFGY (SEQ ID NO: 9). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGAT (SEQ ID NO: 20), and a CDR-H3 comprising the amino acid sequence ARNSGSYSFGY (SEQ ID NO: 9). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT

(SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARASGSYSFGY (SEQ ID NO: 23). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARNSGSASFGY (SEQ ID NO: 25). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence AANSGSYSFGY (SEQ ID NO: 26). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARNAGSYSFGY (SEQ ID NO: 28). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARNSASYSFGY (SEQ ID NO: 30). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARNSGAYSFGY (SEQ ID NO: 32). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARNSGSYAFGY (SEQ ID NO: 34). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARNSGSYSAGY (SEQ ID NO: 36). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARNSGSYSFAY (SEQ ID NO: 38). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARNSGSYSFGA (SEQ ID NO: 40). In some embodiments, the VL domain of the first antigen binding domain comprises a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 12). In some embodiments, the VL domain of the first antigen binding domain comprises a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence QQAASFPFT (SEQ ID NO: 41). In some embodiments, the VL domain of the first

antigen binding domain comprises a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence QQAFSFPFT (SEQ ID NO: 42). In some embodiments, the VL domain of the first antigen binding domain comprises a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence AQAYSFPFT (SEQ ID NO: 43). In some embodiments, the VL domain of the first antigen binding domain comprises a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence QAAYSFPFT (SEQ ID NO: 44). In some embodiments, the VL domain of the first antigen binding domain comprises a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence QQAYAFPFT (SEQ ID NO: 45). In some embodiments, the VL domain of the first antigen binding domain comprises a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence QQAYSAPFT (SEQ ID NO: 46). In some embodiments, the VL domain of the first antigen binding domain comprises a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence QQAYSFAFT (SEQ ID NO: 47). In some embodiments, the VL domain of the first antigen binding domain comprises a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence QQAYSFPAT (SEQ ID NO: 48). In some embodiments, the VL domain of the first antigen binding domain comprises a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence QQAYSFPFA (SEQ ID NO: 49). In some embodiments, the VH domain of the first antigen binding domain comprises: a CDR-H1 comprising the amino acid sequence of GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence of INPNEGDT (SEQ ID NO: 202), and a CDR-H3 comprising the amino acid sequence of ARNTGAYSFGY (SEQ ID NO: 205); and wherein the VL domain of the first antigen binding domain comprises: a CDR-L1 comprising the amino acid sequence of QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence of GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence of QQAYGFPFT (SEQ ID NO: 207). In some embodiments, the VH domain of the first antigen binding domain comprises: a CDR-H1 comprising the amino acid sequence of GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence of INPNEGDT (SEQ ID NO: 202), and a CDR-H3 comprising the amino acid sequence of ARNTGAYSFGY (SEQ ID NO: 205); and wherein the VL domain of the first antigen binding domain comprises: a CDR-L1 comprising the amino acid sequence of QGISSW (SEQ ID NO: 10), a CDR-L2

comprising the amino acid sequence of GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence of HQAYSFPFT (SEQ ID NO: 208).

[0032] In some embodiments, provided herein is a multispecific binding molecule, comprising: (a) a first antibody or antigen binding fragment thereof comprising a first antigen-binding domain, wherein the first antigen binding domain binds to human Dectin-1; and (b) a second antibody or antigen-binding fragment thereof comprising a second antigen binding domain, wherein the second antigen binding domain binds to a target of interest; wherein the first antigen binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain of the first antigen binding domain comprises: a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13) or GYTFTAY (SEQ ID NO:18); a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14) or NPNSGA (SEQ ID NO: 21); and a CDR-H3 comprising an amino acid sequence selected from the group consisting of NSGSYSFGY (SEQ ID NO: 15), ASGSYSFGY (SEQ ID NO: 22), NSGSASFGY (SEQ ID NO: 24), NAGSYSFGY (SEQ ID NO: 27), NSASYSFGY (SEQ ID NO: 29), NSGAYSFGY (SEQ ID NO: 31), NSGSYAFGY (SEQ ID NO: 33), NSGSYSAGY (SEQ ID NO: 35), NSGSYSFAY (SEQ ID NO: 37), and NSGSYSFGA (SEQ ID NO: 39); and wherein the VL domain of the first antigen binding domain comprises: a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4); a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising an amino acid sequence selected from the group consisting of QQAYSFPFT (SEQ ID NO: 6), QQAASFPFT (SEQ ID NO: 41), QQAFSFPFT (SEQ ID NO: 42), AQAYSFPFT (SEQ ID NO: 43), QAAYSFPFT (SEQ ID NO: 44), QQAYAFPFT (SEQ ID NO: 45), QQAYSAPFT (SEQ ID NO: 46), QQAYSFAFT (SEQ ID NO: 47), QQAYSFPAT (SEQ ID NO: 48), and QQAYSFPFA (SEQ ID NO: 49). In some embodiments, the first antigen binding domain does not comprise a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 15), a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the VH domain of the first antigen binding domain comprises: a CDR-H1 comprising the amino acid sequence of DYYM (SEQ ID NO: 199), a CDR-H2 comprising the amino acid sequence of WINPNEGDTNYAQKFEG (SEQ ID NO: 200), and a CDR-H3 comprising the amino acid sequence of NTGAYSFGY (SEQ ID NO: 204); and wherein the VL domain of the first antigen binding domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASDLQS (SEQ ID NO: 206), and a CDR-L3 comprising the amino acid sequence of QQAYGFPFT (SEQ ID NO: 207). In some embodiments, the VH domain of the first antigen binding domain comprises: a CDR-H1 comprising the amino acid sequence of DYYM (SEQ ID NO: 199), a CDR-H2 comprising the amino acid sequence of WINPNEGDTNYAQKFQE (SEQ ID NO: 201), and a CDR-H3 comprising the amino acid sequence of NTGAYSFGY (SEQ ID NO: 204); and wherein the VL domain of the first

antigen binding domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASDLQS (SEQ ID NO: 206), and a CDR-L3 comprising the amino acid sequence of HQAYSFPFT (SEQ ID NO: 208).

[0033] In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 15). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence GYTFTAY (SEQ ID NO:18), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 15). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGA (SEQ ID NO: 21), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 15). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence ASGSYSFGY (SEQ ID NO: 22). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence NAGSYSFGY (SEQ ID NO: 27). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence NSASYSFGY (SEQ ID NO: 29). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence NSGAYSFGY (SEQ ID NO: 31). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence NSGSYAFGY (SEQ ID NO: 33). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence NSGSYSAGY (SEQ ID NO: 35). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence NSGSYSFAY (SEQ ID NO: 37). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence

NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence NSGSYSFGA (SEQ ID NO: 39). In some embodiments, the VL domain of the first antigen binding domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the VL domain of the first antigen binding domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAASFPFT (SEQ ID NO: 41). In some embodiments, the VL domain of the first antigen binding domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAFSFPFT (SEQ ID NO: 42). In some embodiments, the VL domain of the first antigen binding domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence AQAYSFPFT (SEQ ID NO: 43). In some embodiments, the VL domain of the first antigen binding domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QAAYSFPFT (SEQ ID NO: 44). In some embodiments, the VL domain of the first antigen binding domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYAFPFT (SEQ ID NO: 45). In some embodiments, the VL domain of the first antigen binding domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSAPFT (SEQ ID NO: 46). In some embodiments, the VL domain of the first antigen binding domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFAFT (SEQ ID NO: 47). In some embodiments, the VL domain of the first antigen binding domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPAT (SEQ ID NO: 48). In some embodiments, the VL domain of the first antigen binding domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFA (SEQ ID NO: 49). In some embodiments, the VH domain of the first antigen binding domain comprises: a CDR-H1 comprising the amino acid sequence of GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence of NPNEGD (SEQ ID NO: 203), and a CDR-H3 comprising the amino acid sequence of NTGAYSFGY (SEQ ID NO: 204); and wherein the VL domain of

the first antigen binding domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASDLQS (SEQ ID NO: 206), and a CDR-L3 comprising the amino acid sequence of QQAYGFPFT (SEQ ID NO: 207)

[0034] In some embodiments, the VH domain of the first antigen binding domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos:62 and 82-93. In some embodiments, In some embodiments according to any of the embodiments described herein, the VL domain of the first antigen binding domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos: 64 and 94-102. In some embodiments, the VH domain of the first antigen binding domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos:62 and 82-93 and/or the VL domain of the first antigen binding domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos: 64 and 94-102. In some embodiments, the first antigen binding domain does not comprise a VH domain comprising the amino acid sequence of SEQ ID NO:62 and a VL domain comprising the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:82, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid

sequence of SEQ ID NO:82, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:83, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:83, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain of the first antigen

binding domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:84, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:84, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:85, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:85, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the

VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:86, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:86, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID

NO:101. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:87, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:87, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:88, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:88, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain of the first antigen binding domain comprises the

amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:89, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:89, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:90, and the VL domain of the first

antigen binding domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:90, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:91, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:91, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 91,

and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:92, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:92, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:93, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:93, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid

sequence of SEQ ID NO: 93, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 209, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:210. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 211, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:212. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 213, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:214. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 220, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:221. In some embodiments, the first antibody heavy chain comprises a C→S substitution at position 5, according to IMGT hinge numbering, and wherein the first antibody light chain comprises a C→S substitution at the terminal residue of the light chain constant domain. In some embodiments, the first antibody heavy chain comprises the amino acid sequence of SEQ ID NO:219, and wherein the first antibody light chain comprises the amino acid sequence of SEQ ID NO:223.

[0035] In some embodiments, provided herein is a multispecific binding molecule, comprising: (a) a first antibody or antigen binding fragment thereof comprising a first antigen-binding domain, wherein the first antigen binding domain binds to human Dectin-1; and (b) a second antibody or antigen binding fragment thereof comprising a second antigen binding domain, wherein the second antigen binding domain binds to a target of interest; wherein the first antigen binding domain comprises a heavy chain

variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain of the first antigen binding domain comprises the amino acid sequence QVQLVQSGAEVKKPGASVKVSCKX$_1$SGYTFTX$_2$YYX$_3$HWVRQAPGQGLEWMGWINPNSGX$_4$TNYAQKFQGRX$_5$TMTRDTSISTAYX$_6$ELSRLRSDDTAVX$_7$YCARNSGSYSFGYWGQGTLVTVSS; wherein X$_1$ is S or A; wherein X$_2$ is D or G; wherein X$_3$ is I or M; wherein X$_4$ is D or G; wherein X$_5$ is I or V; wherein X$_6$ is L or M; and wherein X$_7$ is F or Y (SEQ ID NO:80); and wherein the VL domain of the first antigen binding domain comprises the amino acid sequence DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIX$_1$X$_2$ASSLQSGVPSRFSGSGSGTDFTLTX$_3$SSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE; wherein X$_1$ is F or Y; wherein X$_2$ is G or A; and wherein X$_3$ is V or I (SEQ ID NO:81). In some embodiments, the first antigen binding domain does not comprise a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3), a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6).

[0036] In some embodiments, provided herein is a multispecific binding molecule, comprising: (a) a first antibody or antigen binding fragment thereof comprising a first antigen binding domain, wherein the first antigen binding domain binds to human Dectin-1; and (b) a second antibody or antigen binding fragment thereof comprising a second antigen binding domain, wherein the second antigen binding domain binds to a target of interest; wherein the first antigen binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain of the first antigen binding domain comprises: a CDR-H1 comprising an amino acid sequence selected from the group consisting of DYYI (SEQ ID NO: 1), DYYM (SEQ ID NO: 66), and GYYM (SEQ ID NO: 67); a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2) or WINPNSGGTNYAQKFQG (SEQ ID NO: 70); and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3); and wherein the VL domain of the first antigen binding domain comprises: a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4); a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5) or AASSLQS (SEQ ID NO: 73), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the first antigen binding domain does not comprise a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3), a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2

comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence DYYM (SEQ ID NO: 66), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence GYYM (SEQ ID NO: 67), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence DYYM (SEQ ID NO: 66), a CDR-H2 comprising the amino acid sequence WINPNSGGTNYAQKFQG (SEQ ID NO: 70), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence GYYM (SEQ ID NO: 67), a CDR-H2 comprising the amino acid sequence WINPNSGGTNYAQKFQG (SEQ ID NO: 70), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3). In some embodiments, the VH domain of the first antigen binding domain further comprises a FR1 comprising an amino acid sequence selected from the group consisting of QVQLVQSGAEVKKPGASVKVSCKSSGYTFT (SEQ ID NO:50) and QVQLVQSGAEVKKPGASVKVSCKASGYTFT (SEQ ID NO:76); a FR2 comprising the amino acid sequence HWVRQAPGQGLEWMG (SEQ ID NO:52); a FR3 comprising an amino acid sequence selected from the group consisting of RITMTRDTSISTAYLELSRLRSDDTAVFYCAR (SEQ ID NO:53) and RVTMTRDTSISTAYMELSRLRSDDTAVYYCAR (SEQ ID NO:77); and a FR4 comprising the amino acid sequence WGQGTLVTVSS (SEQ ID NO:55). In some embodiments, the VL domain of the first antigen binding domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the VL domain of the first antigen binding domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence AASSLQS (SEQ ID NO: 73), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the VL domain of the first antigen binding domain further comprises a FR1 comprising the amino acid sequence DIQMTQSPSSVSASVGDRVTITC (SEQ ID NO:56); a FR2 comprising an amino acid sequence selected from the group consisting of WYQQKPGKAPKLLIF (SEQ ID NO:57) and WYQQKPGKAPKLLIY (SEQ ID NO:78); a FR3 comprising an amino acid sequence selected from the group consisting of GVPSRFSGSGSGTDFTLTVSSLQPEDFATYYC (SEQ ID NO:59) and GVPSRFSGSGSGTDFTLTISSLQPEDFATYYC (SEQ ID NO:79); and a FR4 comprising the amino acid sequence FGPGTKVDIE (SEQ ID NO:61).

[0037] In some embodiments, provided herein is a multispecific binding molecule, comprising: (a) a first antibody or antigen binding fragment thereof comprising a first antigen binding domain, wherein the first antigen binding domain binds to human Dectin-1; and (b) a second antibody or antigen binding fragment thereof comprising a second antigen binding domain, wherein the second antigen binding domain binds to a target of interest; wherein the first antigen binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain of the first antigen binding domain comprises: a CDR-H1 comprising an amino acid sequence selected from the group consisting of GYTFTDYY (SEQ ID NO:7), and GYTFTGYY (SEQ ID NO:68); a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8) or INPNSGGT (SEQ ID NO:71); and a CDR-H3 comprising the amino acid sequence ARNSGSYSFGY (SEQ ID NO: 9); and wherein the VL domain of the first antigen binding domain comprises: a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10); a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11) or AAS (SEQ ID NO: 74), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 12). In some embodiments, the first antigen binding domain does not comprise a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), a CDR-H3 comprising the amino acid sequence ARNSGSYSFGY (SEQ ID NO: 9), a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 12). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARNSGSYSFGY (SEQ ID NO: 9). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence GYTFTGYY (SEQ ID NO:68), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARNSGSYSFGY (SEQ ID NO: 9). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGGT (SEQ ID NO:71), and a CDR-H3 comprising the amino acid sequence ARNSGSYSFGY (SEQ ID NO: 9). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence GYTFTGYY (SEQ ID NO:68), a CDR-H2 comprising the amino acid sequence INPNSGGT (SEQ ID NO:71), and a CDR-H3 comprising the amino acid sequence ARNSGSYSFGY (SEQ ID NO: 9). In some embodiments, the VL domain of the first antigen binding domain comprises a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 12). In some embodiments, the VL domain of the first antigen binding domain comprises a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a

CDR-L2 comprising the amino acid sequence AAS (SEQ ID NO: 74), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 12).

[0038] In some embodiments, provided herein is a multispecific binding molecule, comprising: (a) a first antibody or antigen binding fragment thereof comprising a first antigen binding domain, wherein the first antigen binding domain binds to human Dectin-1; and (b) a second antibody or antigen binding fragment thereof comprising a second antigen binding domain, wherein the second antigen binding domain binds to a target of interest; wherein the first antigen binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain of the first antigen binding domain comprises: a CDR-H1 comprising an amino acid sequence selected from the group consisting of GYTFTDY (SEQ ID NO:13), and GYTFTGY (SEQ ID NO:69); a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14) or NPNSGG (SEQ ID NO: 72); and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 15); and wherein the VL domain of the first antigen binding domain comprises: a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4); a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5) or AASSLQS (SEQ ID NO: 75), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the first antigen binding domain does not comprise a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 15), a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 15). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence GYTFTGY (SEQ ID NO:69), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 15). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGG (SEQ ID NO: 72), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 15). In some embodiments, the VH domain of the first antigen binding domain comprises a CDR-H1 comprising the amino acid sequence GYTFTGY (SEQ ID NO:69), a CDR-H2 comprising the amino acid sequence NPNSGG (SEQ ID NO: 72), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 15). In some embodiments, the VL domain of the first antigen binding domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the VL domain of the first antigen binding

domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence AASSLQS (SEQ ID NO: 75), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6).

[0039] In some embodiments, the VH domain of the first antigen binding domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos: 62 and 103-109. In some embodiments, the VL domain of the first antigen binding domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos:64 and 110-113. In some embodiments, the VH domain of the first antigen binding domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos: 62 and 103-109 and/or the VL domain of the first antigen binding domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos:64 and 110-113. In some embodiments, the first antigen binding domain does not comprise a VH domain comprising the amino acid sequence of SEQ ID NO:62 and a VL domain comprising the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 62, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:110. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 62, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:111. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 62, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:112. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 62, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:113. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 103, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 103, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:110. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 103, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:111. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 103, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:112. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 103, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:113. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 104, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 104, and the VL domain of

the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:110. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 104, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:111. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 104, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:112. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 104, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:113. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 105, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 105, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:110. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 105, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:111. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 105, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:112. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 105, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:113. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 106, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 106, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:110. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 106, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:111. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 106, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:112. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 106, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:113. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 107, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 107, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:110. In some embodiments, the VH domain of the

first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 107, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:111. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 107, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:112. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 107, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:113. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 108, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 108, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:110. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 108, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:111. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 108, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:112. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 108, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:113. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 109, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 109, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:110. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 109, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:111. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 109, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:112. In some embodiments, the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 109, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:113.

[0040] In some embodiments, provided herein is a multispecific binding molecule, comprising: a first arm comprising a single chain variable fragment (scFv) that binds to human Dectin-1 and a first Fc region, wherein the scFv comprises a first VH domain and a first VL domain, and a second arm that comprises a second antibody comprising a second antigen binding domain and a second Fc region, wherein the second antigen binding domain binds to a target of interest; wherein the VH domain of the first antibody arm comprises the amino acid sequence of SEQ ID NO:220, and wherein the VL domain of the first antibody

arm comprises the amino acid sequence of SEQ ID NO:221. In some embodiments, the scFv comprises the amino acid sequence of SEQ ID NO:222. In some embodiments, the first arm comprises the amino acid sequence of SEQ ID NO:224 or 225.

[0041] In some embodiments, provided herein is a multispecific binding molecule, comprising: a first arm comprising a first antibody heavy chain and a first antibody light chain, wherein the first antibody heavy chain comprises a first VH domain and a first Fc region, wherein the first antibody light chain comprises a first VL domain, and wherein the first VH and VL domains form a first antigen binding domain that binds to human Dectin-1; and a second arm comprising a second antibody heavy chain and a second antibody light chain, wherein the second antibody heavy chain comprises a second VH domain and a second Fc region, wherein the second antibody light chain comprises a second VL domain, and wherein the second VH and VL domains form a second antigen binding domain that binds to a target of interest; wherein the first VH domain comprises the amino acid sequence of SEQ ID NO:209 and the first VL domain comprises the amino acid sequence of SEQ ID NO:210. In some embodiments, provided herein is a multispecific binding molecule, comprising: a first arm comprising a first antibody heavy chain and a first antibody light chain, wherein the first antibody heavy chain comprises a first VH domain and a first Fc region, wherein the first antibody light chain comprises a first VL domain, and wherein the first VH and VL domains form a first antigen binding domain that binds to human Dectin-1; and a second arm comprising a second antibody heavy chain and a second antibody light chain, wherein the second antibody heavy chain comprises a second VH domain and a second Fc region, wherein the second antibody light chain comprises a second VL domain, and wherein the second VH and VL domains form a second antigen binding domain that binds to a target of interest; wherein the first VH domain comprises the amino acid sequence of SEQ ID NO:220 and the first VL domain comprises the amino acid sequence of SEQ ID NO:221. In some embodiments, the first antibody heavy chain comprises a C→S substitution at position 5, according to IMGT hinge numbering, and wherein the first antibody light chain comprises a C→S substitution at the terminal residue of the light chain constant domain. In some embodiments, the first antibody heavy chain comprises the amino acid sequence of SEQ ID NO:219, and wherein the first antibody light chain comprises the amino acid sequence of SEQ ID NO:223.

[0042] In some embodiments, the target of interest is a disease-causing agent. In some embodiments, the disease-causing agent is a bacterial cell, fungal cell, virus, senescent cell, tumor cell, protein aggregate (*e.g.*, amyloid beta, or lambda or kappa light chain amyloids), LDL particle, mast cell, eosinophil, ILC2 cell, or inflammatory immune cell. In some embodiments, the target of interest is an antigen expressed on the surface of the bacterial cell, fungal cell, senescent cell, tumor cell, mast cell, eosinophil, ILC2 cell, or inflammatory immune cell. In some embodiments, the target of interest is a surface antigen of the virus. In some embodiments, the target of interest is CD70, HER2, DLL3, NECTIN-4, TROP-2, Mesothelin, LIV-1, C-MET, FOLR1, CD20, CCR8, CD33, or EGFR. In some embodiments, the first antigen-binding domain: binds to human Dectin-1 expressed on the surface of a macrophage, monocyte, dendritic cell, or granulocyte; binds to human Dectin-1 expressed on the surface of a cell with an EC50 of less than 2nM; is

capable of binding human or cynomolgus Dectin-1; and/or does not compete with a native ligand of human Dectin-1. In some embodiments, the second antigen-binding domain binds to CD20 and comprises a VH domain comprising the sequence of SEQ ID NO:129 and a VL domain comprising the sequence of SEQ ID NO:130. In some embodiments, the second antigen-binding domain binds to Trop-2 and comprises a VH domain comprising the sequence of SEQ ID NO:139 and a VL domain comprising the sequence of SEQ ID NO:140. In some embodiments, the second antigen-binding domain binds to light chain amyloid and comprises a VH domain comprising the sequence of SEQ ID NO:143 and a VL domain comprising the sequence of SEQ ID NO:144. In some embodiments, one or both of the first and second antibodies or fragments are human or humanized antibodies or fragments. In some embodiments, one or both of the first and second antibodies or fragments are Fab, Fab', F(ab')2, Fv, Fab'-SH, F(ab')2, single chain antibodies, nanobodies, or scFv fragments. In some embodiments, one or both of the first and second antibodies or fragments further comprise an Fc domain. In some embodiments, the first antibody or fragment is a Fab fragment, and wherein the second antibody or fragment is a full-length antibody, *e.g.*, that comprises an antibody heavy chain and an antibody light chain. In some embodiments, the first and the second antibodies or fragments are both full-length antibodies, *e.g.*, that each comprise an antibody heavy chain and an antibody light chain. In some embodiments, the multispecific binding molecule comprises a first antibody arm comprising a single chain variable fragment (scFv) comprising the VH and VL domains that bind to human Dectin-1 and a first Fc region, and a second antibody arm comprising an antibody heavy chain that comprises the VH domain of the second antigen binding domain in association with an antibody light chain that comprises the VL domain of the second antigen binding domain and a second Fc region connected to the VH domain of the second antigen binding domain. In some embodiments, the first Fc region comprises one or more knob-forming mutations, and the second Fc region comprises one or more cognate hole-forming mutations, or wherein the second Fc region comprises one or more knob-forming mutations, and the first Fc region comprises one or more cognate hole-forming mutations. In some embodiments, the first Fc region comprises a T366W substitution, and the second Fc region comprises T366S, L368A, and Y407V substitutions, according to EU numbering. In some embodiments, the first antibody arm comprises a first linker between the VH and VL domains, and a second linker between the VL domain and the first Fc region. In some embodiments, the first linker comprises one or more repeats of the sequence GGGGS (SEQ ID NO:115). In some embodiments, the first linker comprises the sequence GGGGSGGGGSGGGGS (SEQ ID NO:116) or GGGGSGGGGSGGGGSGGGGS (SEQ ID NO:117). In some embodiments, the second linker comprises the sequence EPKRSDKTHTCPPC (SEQ ID NO:118) or SATHTCPPC (SEQ ID NO:119). In some embodiments, the first antibody or fragment is coupled to avidin, streptavidin, neutravidin, or a biotin-binding derivative thereof, and the second antibody or fragment is coupled to biotin or an avidin-binding derivative thereof; or wherein the second antibody or fragment is coupled to avidin, streptavidin, neutravidin, or a biotin-binding derivative thereof, and the first antibody or fragment is coupled to biotin or an avidin-binding derivative thereof; and wherein the first antibody or fragment is

bound to the second antibody or fragment via an interaction between the avidin, streptavidin, neutravidin, or biotin-binding derivative thereof and the biotin or avidin-binding derivative thereof. In some embodiments, the first antibody or fragment is a Fab fragment coupled to monomeric streptavidin (mSA), and wherein the second antibody or fragment is a biotinylated antibody that comprises an antibody heavy chain and an antibody light chain. In some embodiments, the first antibody or fragment is a full-length antibody coupled to monomeric streptavidin (mSA), and wherein the second antibody or fragment is a biotinylated full-length antibody. In some embodiments, the multispecific binding molecule comprises a first IgG antibody comprising the first antigen binding domain covalently linked to a second IgG antibody comprising the second antigen binding domain. In some embodiments, the multispecific binding molecule comprises a first antibody arm comprising a first antibody heavy chain that comprises the VH domain of the first antigen binding domain and a first Fc region and a first antibody light chain comprising the VL domain of the first antigen binding domain, and a second antibody arm comprising a second antibody heavy chain that comprises the VH domain of the second antigen binding domain and a second Fc region and a second antibody light chain comprising the VL domain of the second antigen binding domain, wherein the first Fc region comprises one or more knob-forming mutations, and the second Fc region comprises one or more cognate hole-forming mutations. In some embodiments, the first Fc region comprises a T366W substitution, and wherein the second Fc region comprises T366S, L368A, and Y407V substitutions, according to EU numbering. In some embodiments, the multispecific binding molecule comprises a first antibody arm comprising the VH domain of the first antigen binding domain and a first Fc region and a second antibody arm comprising the VH domain of the second antigen binding domain and a second Fc region, wherein the first Fc region comprises one or more hole-forming mutations, and the second Fc region comprises one or more cognate knob-forming mutations. In some embodiments, the first Fc region comprises T366S, L368A, and Y407V substitutions, and wherein the second Fc region comprises a T366W substitution, according to EU numbering. In some embodiments, the multispecific binding molecule comprises two antibody Fc regions, and wherein each of the antibody heavy chains comprises an amino acid substitution at one or more of positions 234, 235, and 237, according to EU numbering. In some embodiments, each of the antibody Fc regions comprises L234A, L235E, and G237A substitutions, according to EU numbering. In some embodiments, the Fc region is a human IgG Fc region. In some embodiments, the Fc region is a human IgG1 or human IgG4 Fc region. In some embodiments, the Fc region is a human IgG1 Fc region comprising S239D and I332E substitutions, according to EU numbering. In some embodiments, the Fc region is a human IgG1 Fc region comprising S239D, A330L, and I332E substitutions, according to EU numbering. In some embodiments, the Fc region is a human IgG1 Fc region comprising G236A, S239D, A330L, and I332E substitutions, according to EU numbering. In some embodiments, the Fc region is a human IgG4 Fc region comprising an S228P substitution, according to EU numbering. In some embodiments, the multispecific binding molecule comprises two antibody heavy chains, and wherein only one of the antibody heavy chains comprises H435R and Y436F substitutions, according to EU numbering. In some

embodiments, only one of the antibody arms comprises a heavy chain comprising F126C and C220V substitutions and a light chain comprising S121C and C214V substitutions, according to EU numbering. In some embodiments, the multispecific binding molecule comprises a first antibody heavy chain and a first antibody light chain and a second antibody heavy chain and a second antibody light chain, wherein the VH domain of the first antibody heavy chain forms a first antigen binding domain with the VL domain of the first antibody light chain, wherein the VH domain of the second antibody heavy chain forms a second antigen binding domain with the VL domain of the second antibody light chain, wherein the first antibody heavy chain comprises F126C, C220V, and T366W substitutions, wherein the first antibody light chain comprises S121C and C214V substitutions, and wherein the second antibody heavy chain comprises T366S, L368A, Y407V, H435R, and Y436F substitutions, according to EU numbering. In some embodiments, the first and second antibody heavy chains further comprise L234A, L235E, and G237A substitutions, according to EU numbering. In some embodiments, the first and second antibody heavy chains comprise human IgG1 Fc domains. In some embodiments, at least one or two of the heavy chains of the antibody is/are non-fucosylated or comprise(s) reduced fucosylation. In some embodiments, the antibody may be produced in a cell line having an alpha1,6-fucosyltransferase (Fut8) or alpha-1,3-mannosyl-glycoprotein 2-beta-N-acetylglucosaminyltranferase (MGAT1) knockout. In some embodiments, the antibody may be produced in a cell line overexpressing β1,4-N-acetylglucosaminyltransferase III (GnT-III). In further embodiments, the cell line additionally overexpresses Golgi μ-mannosidase II (ManII). In some embodiments, the antibody may be produced in a cell line treated with an inhibitor of mannosidase I, *e.g.*, kifunensine.

[0043] In some embodiments, provided herein is a polynucleotide encoding the antibody or multispecific binding molecule of any one of the above embodiments. In some embodiments, provided herein is a vector (*e.g.*, an expression vector) comprising the polynucleotide of any one of the above embodiments. In some embodiments, provided herein is a host cell (*e.g.*, an isolated host cell or cell line) comprising the polynucleotide or vector of any one of the above embodiments. In some embodiments, provided herein is a method of producing an antibody or multispecific binding molecule, comprising culturing the host cell of any one of the above embodiments under conditions suitable for production of the antibody or multispecific binding molecule. In some embodiments, the method further comprises recovering the antibody or multispecific binding molecule. In some embodiments, provided herein is a pharmaceutical composition comprising the antibody or multispecific binding molecule of any one of the above embodiments and a pharmaceutically acceptable carrier.

[0044] In some embodiments, provided herein is a method of treating a disease or disorder, comprising administering an effective amount of the antibody, multispecific binding molecule, or composition of any one of the above embodiments to an individual in need thereof. In some embodiments, the first target of interest is human Dectin-1, and wherein the second target of interest is a disease-causing agent. In some embodiments, the disease-causing agent is a bacterial cell, fungal cell, virus, senescent cell, tumor cell, protein aggregate (*e.g.*, amyloid beta, or lambda or kappa light chain amyloids), LDL particle, mast cell,

eosinophil, ILC2 cell, or inflammatory immune cell. In some embodiments, the target of interest is an antigen expressed on the surface of the bacterial cell, fungal cell, senescent cell, tumor cell, mast cell, eosinophil, ILC2 cell, or inflammatory immune cell. In some embodiments, the target of interest is a surface antigen of the virus. In some embodiments, the disease or disorder is cancer, a bacterial infection, a fungal infection, a viral infection, a mast cell disease or disorder, systemic mastocytosis, amyloidosis (*e.g.*, light chain amyloidosis or Alzheimer's disease), or an aging-related disease or disorder. In some embodiments, the target of interest is CD70, HER2, DLL3, NECTIN-4, TROP-2, Mesothelin, LIV-1, C-MET, FOLR1, CD20, CCR8, CD33, or EGFR. In some embodiments, the individual is a human.

[0045] In some embodiments, provided herein is a method of treating cancer, comprising administering an effective amount of a composition comprising a multispecific binding molecule according to any one of the above embodiments to an individual in need thereof, wherein the multispecific binding molecule comprises: (a) a first antibody or antigen-binding fragment thereof comprising a first antigen-binding domain according to any one of the above embodiments, wherein the first antigen-binding domain binds to human Dectin-1; and (b) a second antibody or antigen-binding fragment thereof comprising a second antigen-binding domain, wherein the second antigen binding domain binds to CD70, HER2, DLL3, NECTIN-4, TROP-2, Mesothelin, LIV-1, C-MET, FOLR1, CD20, CCR8, CD33, or EGFR. In some embodiments, the second antigen binding domain binds to human CD70, human HER2, human DLL3, human NECTIN-4, human TROP-2, human Mesothelin, human LIV-1, human C-MET, human FOLR1, human CD20, human CCR8, human CD33, or human EGFR, *e.g.*, as expressed on the surface of a cancer cell.

[0046] In some embodiments, the second antigen binding domain binds to CD20; wherein the second antigen-binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; and wherein the VH domain of the second antigen-binding domain comprises the sequence QVQLQQPGAELVKPGASVKMSCKASGYTFTSYNMHWVKQTPGRGLEWIGAIYPGNGDTSYNQ KFKGKATLTADKSSSTAYMQLSSLTSEDSAVYYCARSTYYGGDWYFNVWGAGTTVTVSA (SEQ ID NO:129) and/or wherein the VL domain of the second antigen-binding domain comprises the sequence QIVLSQSPAILSASPGEKVTMTCRASSSVSYIHWFQQKPGSSPKPWIYATSNLASGVPVRFSGSGS GTSYSLTISRVEAEDAATYYCQQWTSNPPTFGGGTKLEIK (SEQ ID NO:130). In some embodiments, the multispecific binding molecule comprises a first antibody arm comprising the first antigen binding domain and a first Fc region and a second antibody arm comprising the second antigen binding domain and a second Fc region, wherein the first Fc region comprises one or more knob-forming mutations, and the second Fc region comprises one or more cognate hole-forming mutations. In some embodiments, the first Fc region comprises a T366W substitution, and the second Fc region comprises T366S, L368A, and Y407V substitutions, according to EU numbering. In some embodiments, the multispecific binding molecule comprises a first antibody arm comprising the first antigen binding domain and a first Fc region and a second antibody arm comprising the second antigen binding domain and a second Fc region, wherein the first Fc region comprises one or more hole-forming mutations, and

the second Fc region comprises one or more cognate knob-forming mutations. In some embodiments, the first Fc region comprises T366S, L368A, and Y407V substitutions, and the second Fc region comprises a T366W substitution, according to EU numbering. In some embodiments, the antibody comprises two antibody Fc regions, and wherein each of the antibody Fc regions comprises an amino acid substitution at one or more of positions 234, 235, and 237, according to EU numbering. In some embodiments, each of the antibody heavy chains comprises L234A, L235E, and G237A substitutions, according to EU numbering. In some embodiments, the antibody comprises two antibody heavy chains, and wherein only one of the antibody heavy chains comprises H435R and Y436F substitutions, according to EU numbering. In some embodiments, only one of the antibody arms comprises a heavy chain comprising F126C and C220V substitutions and a light chain comprising S121C and C214V substitutions, according to EU numbering. In some embodiments, the bispecific antibody comprises two antibody heavy chains and two antibody light chains, wherein the VH domain of the first antibody heavy chain forms an antigen binding domain with the VL domain of the first antibody light chain, wherein the VH domain of the second antibody heavy chain forms an antigen binding domain with the VL domain of the second antibody light chain, wherein the first antibody heavy chain comprises F126C, C220V, and T366W substitutions, wherein the first antibody light chain comprises S121C and C214V substitutions, and wherein the second antibody heavy chain comprises T366S, L368A, Y407V, H435R, and Y436F substitutions, according to EU numbering. In some embodiments, the first and second antibody heavy chains further comprise L234A, L235E, and G237A substitutions, according to EU numbering. In some embodiments, the first and second antibody heavy chains comprise human IgG1 Fc domains. In some embodiments, the Fc region is a human IgG1 or human IgG4 Fc region. In some embodiments, the Fc region is a human IgG1 Fc region comprising S239D and I332E substitutions, according to EU numbering. In some embodiments, the Fc region is a human IgG1 Fc region comprising S239D, A330L, and I332E substitutions, according to EU numbering. In some embodiments, the Fc region is a human IgG1 Fc region comprising G236A, S239D, A330L, and I332E substitutions, according to EU numbering. In some embodiments, the Fc region is a human IgG4 Fc region comprising an S228P substitution, according to EU numbering. In some embodiments, at least one or two of the heavy chains of the antibody is/are non-fucosylated or comprise(s) reduced fucosylation. In some embodiments, the antibody may be produced in a cell line having an alpha1,6-fucosyltransferase (Fut8) or alpha-1,3-mannosyl-glycoprotein 2-beta-N-acetylglucosaminyltranferase (MGAT1) knockout. In some embodiments, the antibody may be produced in a cell line overexpressing β1,4-N-acetylglucosaminyltransferase III (GnT-III). In further embodiments, the cell line additionally overexpresses Golgi μ-mannosidase II (ManII). In some embodiments, the antibody may be produced in a cell line treated with an inhibitor of mannosidase I, *e.g.*, kifunensine. In some embodiments, the individual is a human.

[0047] In some embodiments, provided herein is a kit or article of manufacture comprising the antibody, multispecific binding molecule, or composition of any one of the above embodiments and instructions for

using the antibody, multispecific binding molecule, or composition according to the method of any one of the above embodiments.

[0048] It is to be understood that one, some, or all of the properties of the various embodiments described herein may be combined to form other embodiments of the present disclosure. These and other aspects of the present disclosure will become apparent to one of skill in the art. These and other embodiments of the present disclosure are further described by the detailed description that follows.

BRIEF DESCRIPTION OF THE DRAWINGS

[0049] **FIGs. 1A-1C** show the binding analysis of the anti-human Dectin-1 antibody (clone 2M24) in human and monkey monocytes derived from peripheral blood mononuclear cells (PBMC) by flow cytometry. Single, live and CD14+ cells were gated to identify monocytes. The cells were incubated with 2M24 anti-Dectin-1 primary antibody or a mIgG1 isotype control antibody, followed by incubation with a fluorescent anti-mouse secondary antibody. The primary antibodies were used in a serial dose titration. **FIG. 1A** shows the binding analysis for anti-human Dectin-1 clone 2M24 in human monocytes. **FIG. 1B** shows the binding analysis for anti-human Dectin-1 clone 2M24 antibody in cynomolgus monocytes. **FIG. 1C** depicts a comparison of binding to human monocytes, HEK cells overexpressing human Dectin-1 and cynomolgus monocytes between the 2M24 clone and other Dectin-1 antibodies identified from the ATX-Gx Alloy transgenic mice immunization as well as commercial anti-Dectin-1 antibodies. Anti-human Dectin-1 clone 2M24 antibody demonstrated high affinity to both human and cynomolgus monkey Dectin-1 expressed in monocytes, and exhibited superior affinity as compared to other anti-Dectin-1 antibodies, including commercial antibodies.

[0050] **FIGs. 2A-2B** show the phagocytosis of pHrodo-labeled polystyrene anti-mouse Fc IgG beads conjugated with anti-Dectin-1 antibody 2M24 or isotype control antibody by HEK-Blue hDectin-1a cells and human monocytes. Polystyrene anti-mouse Fc IgG beads (~ 3.4 μm) were labeled with a pH-sensitive fluorescent dye (pHrodo Red) and conjugated with Dectin-1 antibody 2M24 or isotype control. The beads were then incubated with cultured HEK-Blue hDectin-1a cells or human monocytes at a ratio of 1:2 (cells: beads). HEK-Blue hDectin-1a cells were labeled with the cell-permeant dye Calcein AM. The phagocytosis of the beads was monitored by IncuCyte live cell imaging. Phagocytosis was quantified using the IncuCyte analysis software and expressed as overlap of red object count (pHrodo) to calcein-positive cells. **FIG. 2A** shows the phagocytosis of beads over 2.5 hours in HEK-Blue hDectin-1a cells (top) and representative images of pHrodo positive cells at 2.5 hours of phagocytosis (bottom). **FIG. 2B** shows the phagocytosis of beads over 4 hours in human monocytes (top), as well as representative images of pHrodo positive cells at 2.5 hours of phagocytosis (bottom). In the representative images, engulfed beads fluoresce brightly in phagosomes.

[0051] **FIGs. 3A-3B** show the binding of the fully human 2M24 anti-Dectin-1 antibody (hIgG4) or isotype control antibody in HEK-Blue hDectin-1a cells and primary human monocytes. **FIG. 3A** shows the binding analysis of the fully human 2M24 anti-Dectin-1 antibody to HEK cells, while **FIG. 3B** shows

the binding to primary human monocytes. The primary antibodies were used in a serial dose titration followed by a fluorescent secondary antibody against the primary antibody. The fully human 2M24 anti-Dectin-1 hIgG4 antibody bound with high affinity to Dectin-1 expressing cells.

[0052] **FIG. 4** shows the targeted phagocytosis of pHrodo-labeled polystyrene biotin beads conjugated with the fully human 2M24 anti-Dectin-1 antibody (hIgG4) or isotype control antibody by Dectin-1 expressing cells. Polystyrene biotin beads were labeled with pHrodo Red and conjugated via streptavidin to anti-Dectin-1 antibody 2M24 or an isotype control. The conjugated beads were mixed with cells at a ratio of 1:3, and phagocytosis of the beads was monitored by IncuCyte live cell imaging. The phagocytosis of phrodo-biotin beads conjugated to streptavidin 2M24 anti-Dectin-1 hIgG4 antibody is shown for HEK-Blue hDectin-1a cells (top left), human monocytes (top right) and human macrophages (bottom). The fully human 2M24 anti-Dectin-1 antibody (hIgG4) promoted phagocytosis in Dectin-1 expressing cells.

[0053] **FIGs. 5A-5B** show the results of a secreted alkaline phosphatase reporter assay of Dectin-1 in HEK-Blue hDectin-1a cells. **FIG. 5A** shows the results for a secreted alkaline phosphatase assay performed using immobilized fully human 2M24 anti-Dectin-1 antibody. The fully human 2M24 (hIgG4) anti-Dectin-1 antibody or an isotype control antibody were immobilized overnight in U-bottomed polypropylene microtiter plates at quantities ranging from 0.1 – 10 μg per well, followed by culture of HEK-Blue hDectin-1a cells for 22 hours and evaluation of alkaline phosphatase secretion at OD 630 nm in the supernatant. **FIG. 5B** shows the results for a secreted alkaline phosphatase assay performed using bead-conjugated fully human 2M24 anti-Dectin-1 antibody. Biotin beads of 3, 10 and 16.5 μm in size were conjugated to streptavidin 2M24 (hIgG4) anti-Dectin-1 antibody. Antibody-conjugated beads were mixed with HEK-Blue hDectin-1a cells for 22 hours, and the supernatant was evaluated for alkaline phosphatase secretion at OD 630 nm. Bars represent mean ± s.d.; n = 2 replicates. The 2M24 (hIgG4) anti-Dectin-1 antibody induced alkaline phosphatase secretion in HEK-Blue hDectin-1a cells both in an immobilized form and conjugated to beads.

[0054] **FIGs. 6A-6B** show the cytokine secretion by human primary macrophages stimulated with anti-Dectin-1 (15E2) antibody in solution. Primary human macrophages and primary monocytes were stimulated with 10 μg/ml of the 15E2 anti-Dectin-1antibody or isotype antibody in solution for 24 hours, and secretion of TNFa and IL6 was assessed by ELISA analysis of the supernatant. Zymosan was used as positive controls for cytokine secretion. Bars represent mean ± s.d.; n = 2 replicates **FIG. 6A** shows the results for primary human monocytes stimulated with soluble 15E2 anti-Dectin-1antibody, while **FIG. 6B** shows the results for stimulated primary human macrophages. Soluble 15E2 anti-Dectin-1 antibody did not induce cytokine secretion in primary human monocytes and macrophages.

[0055] **FIGs. 7A-7B** show the cytokine secretion by human primary monocytes and PBMCs stimulated with immobilized 2M24 or 15E2 anti-Dectin-1 antibody. The anti-Dectin-1 antibodies or isotype control antibodies were immobilized overnight in U-bottomed polypropylene microtiter plates at 10 μg per well, followed by culture of human monocytes or human PBMCs for 24 hours. The secretion of TNFa, IL6 and

IFNg was evaluated by ELISA analysis of the supernatant. **FIG. 7A** shows the cytokine secretion by human monocytes following stimulation with immobilized anti-Dectin-1 antibodies, while **FIG. 7B** shows the cytokine secretion by cultured human PBMCs after stimulation. Bars represent mean ± s.d.; n = 2 replicates. The 2M24 anti-Dectin-1 antibody induced cytokine secretion in both primary human monocytes and PBMCs and exhibited superior immune stimulation to the 15E2 Dectin-1 agonistic antibody

[0056] **FIG. 8** shows the results of a competition assay performed using the 12M4 anti-Dectin-1 antibody clone and natural ligands for Dectin-1. HEK-Blue hDectin-1a cells were incubated in a 1/3 serial dose titration of 2M24 (hIgG4) anti-Dectin-1 antibody or the 15E2, 259931, GE2 anti-Dectin-1 commercial antibodies starting at 300 nM and in the presence of 8 ug/ml of biotin-laminarin for 30 minutes on ice. Binding of laminarin to Dectin-1 was assessed by flow cytometry using Streptavidin-Alexa fluor 647. The 2M24 (hIgG4) anti-Dectin-1 antibody did not compete with natural ligand for binding to Dectin-1.

[0057] **FIG. 9** depicts a summary of the functional characterization of the 2M24 and 15E2 anti-Dectin-1 antibodies.

[0058] **FIGs. 10A-10B** show a schematic illustration of bispecific antibody generation by click chemistry. **FIG. 10A** depicts the differential labeling of antibodies with MTA or FOL reagents **FIG. 10B** depicts the covalent crosslinking of antibodies via specific MTA-FOL interactions.

[0059] **FIG. 11A** illustrates the potential modes of activity deployed by anti-Dectin-1 agonistic bispecific antibodies to eliminate target cancer cells. These include immune stimulation, phagocytosis, neo-antigen presentation and activation of T and B lymphocytes of the adaptive immune system.

[0060] **FIG. 11B** shows a list of potential targets for cancer cell depletion.

[0061] **FIGs. 12A-12B** show the characterization of click chemistry-conjugated bispecifics comprising anti-Dectin-1 (clone 2M24) and anti-hCD70 arms. **FIG. 12A** shows an SDS-PAGE analysis of covalently conjugated antibody pairs (2M24/anti-hCD20, 2M24/anti-hCD70, and isotype controls) under non-reducing and reducing conditions. **FIG. 12B** shows a flow cytometry-based characterization of bispecific (2M24/anti-hCD70 or isotype control) binding to Dectin-1-expressing HEK293 cells (top left) and two renal carcinoma cell lines – A498 (top right) and 786-0 (bottom left). **FIG. 12B** also depicts the EC50 concentration (nM) based on a non-linear regression fitting (bottom right). Anti-Dectin-1/anti-hCD70 bispecific binds Dectin-1- or CD70-expressing cells with an affinity of 1.8 nM or 12.34 nM, respectively.

[0062] **FIG. 13** shows coupling of Dectin-1-expressing HEK293 cell line and A498 renal carcinoma cell line induced by 2M24/anti-hCD70 bispecific. Shown are a flow cytometry analysis of co-cultures of HEK293 cells (labeled with calcein green) and A498 cells (labeled with calcein red) in the presence of 2M24/anti-hCD70 bispecific or isotype control (left). Coupling of HEK293 and A498 cells is indicated by a double-positive signal (green+ red+, square box). Also shown is coupling efficiency, which is quantified as the percentage of total target cells (A498) that forms doublets with HEK293 cells (right). Bars

represent mean ± s.d.; n = 3 replicates. The 2M24/anti-hCD70 bispecific antibody induced coupling of Dectin-1-expressing HEK293 cell line and A498 renal carcinoma cell line

[0063] **FIGs. 14A-14B** shows the coupling of Dectin-1-expressing cells and B cells induced by anti-Dectin-1/anti-hCD20 bispecific antibody. **FIG. 14A** shows the coupling of Dectin-1-expressing HEK293 cells and B cells induced by anti-Dectin-1/anti-hCD20 bispecific antibody. Shown are a flow cytometry analysis of co-cultures of HEK293 cells (labeled with calcein green) and Raji cells (labeled with calcein red) in the presence of 2M24/anti-hCD70 bispecific or isotype control (left). Coupling of HEK293 and Raji cells is indicated by a double-positive signal (green+ red+; square box). Also shown is the coupling efficiency, which is quantified as the percentage of total target cells (Raji) that forms doublets with HEK293 cells (right). Bars represent mean ± s.d.; n = 2 replicates. **FIG. 14B** shows the results of similar experiments performed to assess the coupling of human M0 macrophages and Raji cells induced by anti-Dectin-1/anti-hCD20 bispecific. Bars represent mean ± s.d.; n = 2 replicates. The 2M24/anti-hCD20 bispecific induced coupling of Dectin-1-expressing cells and CDC20-positive B cells (Raji cells).

[0064] **FIG. 15** shows the results of a secreted alkaline phosphatase reporter assay by Dectin-1 in HEK-Blue hDectin-1a cells using an anti-Dectin-1/anti-CD20 bispecific in the presence of Raji cells. A 2M24 (hIgG4)/a-CD20 bispecific antibody was incubated with Raji cells, after which it was washed twice to remove unbound bispecific antibody. The Raji cells were then mixed with HEK-Blue hDectin-1a cells at a ratio of 200.000 Raji cells to 100.000 HEK cells for 22 hours. Secreted alkaline phosphatase was evaluated at OD 630 nm in the supernatant. Bars represent mean ± s.d.; n = 2 replicates. Raji cells coated with an anti-Dectin-1/anti CD20 bispecific induced alkaline phosphatase secretion in HEK-Blue hDectin-1a cells.

[0065] **FIG. 16** shows the induction of Raji cell phagocytosis by Dectin-1-expressing HEK 293 cells by anti-Dectin-1/anti-hCD20 bispecific antibodies. Representative Incucyte images illustrating phagocytosis of Raji cells by HEK cells (arrowhead) at 16h versus 0h are shown (left). Co-localization is indicated by yellow fluorescence. Reduction in calcein red signal of Raji cells at 16h indicates phagocytosis-mediated cell death. Quantification of overlap or co-localization of HEK (calcein green) and Raji (calcein red) in different treatment groups are shown (right). Pre-incubation of HEK cells with ADCP inhibitor Latrunculin A blocks phagocytosis mediated by 15E2/anti-hCD20 bispecific antibody. (n = 2 replicates).

[0066] **FIG. 17** shows coupling of Dectin-1- and HER2-expressing cells induced by anti-Dectin-1/anti-hHER2 bispecific antibodies. Shown are a flow cytometry analysis of co-cultures of Dectin-1-expressing HEK 293 cells (labeled with calcein green) and HER2-expressing SKBR3 cells (labeled with pHrodo red) in the presence of 15E2/anti-hHER2 bispecific or isotype control (left). Coupling of HEK 293 and SKBR3 cells is indicated by a double-positive signal (green+ red+; square box). Also shown is the coupling efficiency, which is quantified as the percentage of total target cells (SKBR3) that forms doublets with the Dectin-1 expressing cells (right). Bars represent mean ± s.d.; n = 2 replicates. Anti-Dectin-1/anti-hHER2 bispecific induces coupling of Dectin-1- and HER2-positive cancer cells.

[0067] **FIG. 18** shows coupling of Dectin-1-expressing HEK293 cells and CD94-expressing BaF3 cells induced by anti-Dectin-1/anti-hCD94 bispecific induces. Shown are a flow cytometry analysis of co-cultures of HEK293 cells (labeled with calcein green) and BaF3 cells (labeled with pHrodo red) in the presence of 2M24/anti-hCD94 bispecific or isotype control (left). Coupling of HEK293 and BaF3 cells is indicated by a double-positive signal (green+ red+; square box). Also shown is the coupling efficiency, which is quantified as the percentage of total target cells (BaF3) that forms doublets with HEK293 cells (right). Bars represent mean ± s.d.; n = 2 replicates. Anti-Dectin-1/anti-hCD94 bispecific induced coupling of Dectin-1- and CD94-expressing cells.

[0068] **FIGs. 19A-19B** show a schematic illustration of Fab 2M24-mSA or full length 2M24-mSA bound to a biotinylated target antibody. **FIG. 19A** shows chimeric fusions of monomeric Streptavidin (mSA) and Fab 2M24 or full length 2M24. mSA is genetically fused to either Fab 2M24 or full length 2M24. **FIG. 19B** shows the coupling of Fab 2M24-mSA or 2M24-mSA to biotinylated target antibodies. The chimeric fusions are incubated with biotinylated target antibodies to generate a bispecific comprising a Dectin-1-binding arm and a second arm binding a target receptor or protein of interest.

[0069] **FIGS. 20A-20C** show the biochemical and functional characterization of Fab 2M24-mSA fusion protein. **FIG. 20A** shows an HPLC characterization of recombinant Fab 2M24-mSA. **FIG. 20B** shows an SDS-PAGE analysis of purified Fab 2M24-mSA under reducing conditions. **FIG. 20C** shows a flow cytometry characterization of Fab 2M24-mSA binding to HEK 293 cells stably overexpressing human Dectin-1 (EC_{50} = 1.45 nM). Fab 2M24 fusion to monomeric streptavidin binds to Dectin-1-expressing cells with an affinity of 1.45 nM.

[0070] **FIGs. 21A-21B** shows the phagocytosis of pHrodo-labeled polystyrene biotin beads conjugated with a Fab-2M24 anti-Dectin-1 antibody tagged with monomeric streptavidin (Fab-2M24-mSA). **FIG. 21A** shows duplet formation of HEK-Blue hDectin-1a cells with Fab-2M24-mSA conjugated to biotin beads and phagocytosis of the beads, assessed by flow cytometry. **FIG. 21B** shows the phagocytosis of phrodo biotin beads (~ 3 μm) conjugated to Fab-2M24-mSA assessed by IncuCyte live imaging (top), as well as representative images of pHrodo positive cells at 3 hours of phagocytosis (engulfed beads fluoresce brightly red in phagosomes) vs. no bead controls (bottom). Fab 2M24-mSA fusion induced binding and phagocytosis of beads by Dectin-1-expressing HEK 293 cells.

[0071] **FIGS. 22A-22D** show bispecific complexes comprising Fab 2M24-mSA and target biotinylated antibodies. Depicted are the HPLC analyses of Fab 2M24-mSA in complex with biotinylated anti-hCD20 (**FIG. 22A**), biotinylated anti-hCD19 (**FIG. 22B**), biotinylated anti-hCD70 (**FIG. 22C**), or biotinylated anti-Amyloid β 1-42 (**FIG. 22D**). Each panel contains superposition of A280 traces including Fab 2M24-mSA alone, target biotinylated antibody alone, and Fab 2M24-mSA in complex with biotinylated target antibody.

[0072] **FIG. 23** shows coupling of Dectin-1-expressing HEK293 cells and CD20-expressing Raji cells induced by Fab 2M24-mSA/biotin anti-hCD20 bispecific antibodies. Shown are the flow cytometry

analysis of co-cultures of HEK293 (labeled with calcein green) and Raji (labeled with calcein red) in the presence of Fab 2M24-mSA/biotin anti-hCD20 bispecific or isotype bispecific control (left). Co-cultures were incubated at 4 °C or 37 °C. Coupling of HEK293 and Raji cells is indicated by a double-positive signal (green+ red+; dotted-square). Also shown is the coupling efficiency, which is quantified as the percentage of total target cell (Raji) that forms doublets (right). Bars represent mean ± s.d.; n = 4 replicates. Fab 2M24-mSA/biotin anti-hCD20 bispecific induced coupling of Dectin-1-expressing HEK293 cells and Raji cells.

[0073] **FIG. 24** is a schematic of targeted phagocytosis of amyloid deposits in amyloidosis using Dectin-1 agonistic bispecific antibodies.

[0074] **FIGs. 25A-25B** show strategies for targeted depletion of mast cells using Dectin-1 agonistic bispecific antibodies. **FIG. 25A** is a schematic of depletion of mast cells by Dectin-1 agonistic bispecific antibodies. **FIG. 25B** shows a list of potential targets for mast cell depletion.

[0075] **FIG. 26** shows the phagocytosis of large (~ 16.2 μm) phrodo-labelled beads by human dendritic cells. **FIG. 26** shows the quantification of phagocytosis of beads over 12 hours (left), and representative images of pHrodo positive cells at 3 hours of phagocytosis (engulfed beads fluoresce brightly red in phagosomes; right). Dectin-1 antibody promoted the directed phagocytosis of beads in cultured monocyte-derived dendritic cells.

[0076] **FIG. 27** is a schematic of targeted depletion of microbes by Dectin-1 agonistic bispecific antibodies. Bispecific antibodies with a Dectin-1-binding arm and a microbial agent-binding arm are generated to target bacteria, viruses or fungi (top). The Dectin-1 bispecific antibodies deploy Dectin-1-expressing phagocytes to eliminate bacterial, viral or fungal pathogens (bottom).

[0077] **FIGs. 28A-28B** show binding of bispecific antibodies comprised of Dectin-1 antibody (15E2 clone) conjugated to anti-H3N2 Hemagglutinin antibody (12CA5 clone) to the H3N2 flu virus and to Dectin-1-expressing cells. **FIG. 28A** shows the binding analysis of an anti-Dectin-1/anti-Hemagglutinin bispecific antibody to the H3N2 flu virus as assessed by ELISA. 96 well microtiter plates were coated with the H3N2 flu viral particles followed by incubation of single antibodies, bispecific antibodies and isotype controls. After extensive washing, the primary antibodies were detected with a secondary anti-mouse FcgR HRP antibody. **FIG. 28B** shows the binding analysis of an anti-Dectin-1/anti-Hemagglutinin bispecific antibody to HEK cells expressing Dectin-1 by flow cytometry. HEK cells were incubated with the primary antibodies followed by detection with a secondary fluorescent antibody against the anti-Dectin-1 antibody (anti-mIgG2a APC) or the Hemagglutinin antibody (anti-mIgG2b PB). The anti-Dectin-1/anti-Hemagglutinin bispecific antibody bound efficiently to both the H3N2 flu virus and to HEK cells expressing Dectin-1.

[0078] **FIGs. 29A-29B** show schematic diagrams using anti-Dectin-1 antibodies to deliver antigens for vaccine development, using anti-Dectin-1 antibodies fused to target antigens for delivery to APCs (**FIG.**

29A), or anti-Dectin-1 bispecific antibodies for targeted delivery of disease-causing agents (*e.g.*, cells, microbes, proteins, etc.) to APCs **(FIG. 29B).**

[0079] **FIG. 30** shows the phagocytosis of pHrodo-labeled polystyrene anti-mouse Fc IgG beads (~ 3.4 μm) conjugated with Dectin-1antibody (15E2) or isotype control antibody by human dendritic cells. Polystyrene anti-mouse Fc IgG beads were labeled with a pH-sensitive fluorescent dye (pHrodo Red) and conjugated with a Dectin-1 antibody or isotype control. The beads were then incubated with cultured monocyte-derived dendritic cells at a ratio of 1:3 (cells: beads). Bead phagocytosis was monitored by IncuCyte live cell imaging. Phagocytosis was quantified using the IncuCyte analysis software and expressed as total integrated intensity (total sum fluorescent intensity) of red objects (pHrodo) in the image. **FIG. 30** shows the quantification of phagocytosis of beads over 9 hours (top) and representative images of pHrodo positive cells at 3 hours of phagocytosis (engulfed beads fluoresce brightly red in phagosomes; bottom).

[0080] **FIGs. 31A-31C** show the phagocytosis of SARS-CoV-2 Spike protein-coated beads by Dectin-1-expressing HEK 293 cells. **FIG. 31**A is a schematic illustration of the experiment. Beads coated with the Spike protein from SARS-CoV-2 are coupled to Dectin-1-expressing HEK 293 cells by an anti-Dectin-1 bispecific antibody comprising a Dectin-1 protein binding arm and a Spike protein binding arm. **FIG. 31B** shows a flow cytometry characterization of effector (HEK 293 cells) and target (Spike-coated beads) engagement by the bispecific and isotype controls (panel A), as well as a quantification of coupling efficiency based on doublet population (panel B). **FIG. 31C** shows the phagocytosis of SARS-CoV-2 Spike protein-coated beads by HEK 293 cells in a co-culture experiment. Phagocytosis of pHrodo-labeled beads was monitored by the change in pHrodo fluorescence as a result of acidic pH in phagosomes. **FIG. 31C** shows quantification of phagocytosis (left), which was quantified by the Incucyte analysis software and expressed as overlap of red object count (pHrodo) to calcein-positive cells, as well as representative images of pHrodo-positive cells at 2 hours of phagocytosis (engulfed beads fluoresce brightly red in phagosomes; right).

[0081] **FIGS. 32A & 32B** show a bispecific antibody design for human bispecific antibodies (*e.g.*, human IgG1 bispecific antibodies) targeting Dectin-1 and a disease target or antigen. **FIG. 32A** provides a diagram of the design. One arm (2M24A.X) with VH domain A and VL domain B targets human Dectin-1, while the other arm (2M24B.X) with VH domain C and VL domain D targets a disease target or antigen. **FIG. 32B** provides a diagram of an exemplary mechanism of action for an anti-Dectin-1 bispecific antibody with an active Fc domain, which targets hDectin-1 (via the first arm) on myeloid cells, an antigen on a target cell/disease-causing agent (via the second arm), and Fc receptors on myeloid and NK cells, eliciting robust immune stimulation and phagocytosis.

[0082] **FIGS. 33A & 33B** show that a bispecific antibody with one arm targeting hDectin-1 and the other arm targeting hCD20 (using the variable domains of rituximab) binds to cells expressing human Dectin-1 or human CD20. **FIG. 33A (top panel)** shows binding of the bispecific antibody targeting hDectin-1 and hCD20 (2M24/CD20), or a bispecific antibody targeting hDectin-1 and RSV (2M24/RSV),

to HEK293 cells stably expressing human Dectin-1, as assessed by flow cytometry. **FIG. 33A (bottom panel)** shows binding of the bispecific antibody 2M24/RSV hIgG1-FITC conjugated and 2M24 bivalent hIgG1-FITC conjugated to PBMCs, as assessed by flow cytometry. **FIG. 33B** shows binding of rituximab (human IgG1), 2M24/CD20 with active human IgG1 Fc, 2M24/CD20 with inert human IgG1 Fc, 2M24/RSV with active human IgG1 Fc, or 2M24/RSV with inert human IgG1 Fc to CD20-expressing B cell lymphoma Raji cell line.

[0083] **FIGS. 34A & 34B** show that bispecific antibody targeting hDectin-1 and hCD20 (2M24/CD20) induces coupling of Dectin-1- and CD20-expressing cells. **FIG. 34A**: To assess coupling of Dectin-1-expressing HEK293 cells (effector) and CD20-expressing Raji cells (target), cells were differentially labeled with calcein green (effector) or calcein red (target) dyes. Labeled cells were co-cultured and treated with hIgG1 inert 2M24/CD20 or 2M24/RSV (control) bispecific antibody to induce effector: target coupling. Successful coupling of effector: target cells is indicated by the double-positive staining (Calcein green+, calcein red+, square box). **FIG. 34B**: Dose-titration of bispecifics in co-cultures of effector: target cells. Coupling efficiency is quantified as the percentage of total target cells that binds or couples to effector cells.

[0084] **FIGS. 35A & 35B** show that bispecific antibody targeting hDectin-1 and hCD20 (2M24/CD20) with an active hIgG1 Fc does not induce monocyte depletion by antibody dependent-cellular cytotoxicity (ADCC) or antibody-dependent cellular phagocytosis (ADCP). PBMCs from two healthy donors – donor 76 (**FIG. 35A**) and donor 77 (**FIG. 35B**) were treated with increasing concentrations of 2M24/CD20 bispecific antibody (hIgG1 active or inert isotypes) and rituximab for 24 h, and subsequently analyzed by flow cytometry to quantify the levels of live, CD14+ monocytes remaining (as a % of isotype controls).

[0085] **FIGS. 36A & 36B** show that bispecific antibody targeting hDectin-1 and hCD20 (2M24/CD20) with an active hIgG1 Fc elicits superior B cell depletion compared to Rituximab. PBMCs from two healthy donors – donors 83 (**FIG. 36A**) and 84 (**FIG. 36B**) – were treated with increasing concentrations of the indicated antibodies for 24 h, and subsequently analyzed by flow cytometry to quantify the levels of remaining live, CD19+ B cells (reported as a % of B cells in isotype control-treated PBMCs).

[0086] **FIGS. 37A & 37B** show that Rituximab induces higher B cell shaving (CD19 downregulation) compared to 2M24/CD20 active IgG1 bispecific antibody. Expression of CD19+ on B cells from two healthy donors – donor 83 (**FIG. 37A**) and donor 84 (**FIG. 37B**) – was quantified by flow cytometry following a 24-hour incubation with increasing concentration of 2M24/CD20 hIgG1 (active isotype) bispecific antibody, Rituximab, or isotype controls. The mean fluorescent intensity (MFI) for CD19 staining using anti-CD19 (BV605 conjugated) was used to evaluate the effect of 2M24/CD20 bispecific and Rituximab on CD19 expression on B cells. EC50 values were calculated based on non-linear regression analysis.

[0087] **FIG. 38** shows differential cytokine release induced by 2M24/CD20 active IgG1 bispecific antibody as compared to rituximab. ELISA-based (mesoscale discovery) quantification of cytokines was undertaken in supernatants isolated from healthy donor PBMCs treated with 2M24/CD20 active hIgG1

bispecific, Rituximab, or isotype controls. PBMCs were stimulated with antibodies overnight, and supernatants were subsequently analyzed by MSD. Cytokines tested were IFNγ, IL-12p70, IL-6, TNFα, IL-1β, IL-4, IL-13, IL-10, and IL-8. Each plot shows cytokine secretion (in pg/mL) as a function of antibody used for treatment (from left to right: 2M24/CD20 hIgG1 bispecific, 2M24/RSV hIgG1 bispecific, rituximab hIgG1, and isotype control hIgG1).

[0088] **FIGS. 39A & 39B** show that 2M24/CD20 hIgG1 (active isotype) bispecific antibody induces superior B-cell depletion and lower CD19 shaving compared to Rituximab in co-cultures of human macrophages and GFP-expressing Raji B cells. **FIG. 39A**: Flow cytometry analysis of co-cultures of human macrophages and Raji-GFP cells (3:1 ratio) in the presence of 2M24/CD20 hIgG1 (active isotype) bispecific, 2M24/RSV control, fucosylated Rituximab or isotype hIgG1 control. Co-cultures were incubated at 37°C for 24 hours and then stained with a PE a-CD206 Ab to label macrophages and a BV-605 a-CD19 antibody to label Raji cells. The number of the remaining live/Raji-GFP+ cells was assessed in the end of the experiment. The primary antibodies were used in a serial dose titration. **FIG. 39B**: Assessment of CD19 on Raji-GFP cells after 24 hours. B-cell receptor shaving is shown as the reduction in the CD19 MFI in the presence of a-Dectin-1/a-hCD20 bispecific or Rituximab.

[0089] **FIGS. 40A-40C** show that 2M24/CD20 active IgG1 bispecific antibody induces superior tissue B cell depletion as compared to Rituximab in single cell suspension of kidney cancer biopsies. Single cell suspensions from two Kidney cancer tissue biopsies were analyzed by flow cytometry in the presence of 2M24/CD20 hIgG1 (active or inert) bispecific antibody, 2M24/RSV hIgG1 controls, fucosylated Rituximab, and respective isotype controls. Kidney cancer tissue biopsies were dissociated to single cell suspensions and treated with primary antibodies (2 μg/ml) for 24 hours at 37°C. Immune cell populations were analyzed by flow cytometry. Cells were initially gated for live cells, further separated into CD45+ cells (immune cells) and CD45- cells (non-immune cells), and then CD19+ (B cells) and CD3+ (T Cells) cells were identified within the CD45+ population **(FIGS. 40A & 40B)**. The number of the remaining B cells was assessed by an anti-CD19 antibody and expressed as percentage of the CD45+ immune cell population (**FIG. 40C**).

[0090] **FIGS. 41A-41C** show that Anti-Dectin 1 antibody (clone 2M24) induces Dectin 1-clustering and TNFα secretion from human macrophages. Cytokine secretion by cultured macrophages and single cell suspension of kidney cancer biopsies stimulated with immobilized anti-Dectin-1 antibody (clone 2M24) or 2M24/CD20 bispecific antibody was tested. The anti-Dectin-1 antibody (clone 2M24), isotype control or the 2M24/CD20 bispecific antibody were immobilized overnight in U-bottomed polypropylene microtiter plates at 10 ug per well, followed by culture of human monocyte-derived macrophages (**FIGS. 41A & 41B**) or single cell suspension from kidney cancer biopsy (**FIG. 41C**). The cells were cultured for 24 hours and evaluation of TNFα secretion in the supernatant was assessed by ELISA. As a positive control, cells were stimulated with zymosan.

[0091] **FIG. 42** shows that immobilized anti-Dectin 1 antibody (clone 2M24) promotes immune stimulation in single cell suspension of kidney cancer biopsies. Single-cell suspensions from kidney

cancer biopsies were treated with immobilized anti-Dectin-1 antibody (clone 2M24) or isotype control hIgG4 antibody for 24 h. Supernatants were analyzed by ELISA for the release of various cytokines, including IFNγ, IL-6, TNFα, IL-23, IL-12p70, IL-10, and IL-13. Each plot shows amount of cytokine (pg/mL) as a function of antibody treatment. Shown are results from treatment with anti-Dectin-1 antibody (clone 2M24) or isotype control hIgG4 antibody using kidney cancer donor 3 (left) or donor 4 (right).

[0092] **FIG. 43** shows the effect of 2M24/CD20 bispecific antibody on CD16 expression in human NK cells, as compared to rituximab or isotype control (RSV). Results indicate that CD16 antigen levels on NK cells are better maintained in PBMCs treated with the 2M24/CD20 bispecific compared to rituximab.

[0093] **FIG. 44** shows the effect of 2M24/CD20 bispecific antibody on CD19 expression in human B cells, as compared to rituximab or isotype control (2M24/RSV bispecific). Results indicate that CD19 antigen levels are better maintained on B cells treated with the 2M24/CD20 bispecific compared to rituximab.

[0094] **FIG. 45** shows depletion of human B cells by 2M24/CD20 bispecific antibody derived from rituximab or 2M24/CD20 bispecific antibody derived from obinutuzumab. Results indicate that the 2M24/CD20 bispecific derived from the rituximab arm is better at depleting B cells compared to the bispecific derived from obinutuzumab.

[0095] **FIG. 46** shows the design of an exploratory study on safety and efficacy of 2M24/CD20 bispecific antibody in non-human primates.

[0096] **FIGS. 47 & 48** show depletion of circulating B cells in cynomolgus monkeys by 2M24/CD20 hIgG1 bispecific antibody generated in cells treated with kifunensine (KIF). **FIG. 47**: B cell depletion in monkeys treated with 5mg/kg 2M24/CD20 hIgG1 KIF (upper) or 2M24/CD20 hIgG1 inert (lower). **FIG. 48**: B cell depletion in monkeys treated with 5mg/kg rituximab hIgG1 KIF.

[0097] **FIGS. 49A & 49B** show depletion of tissue-resident B cells in cynomolgus monkeys by 2M24/CD20 hIgG1 bispecific antibody generated in cells treated with kifunensine (KIF). **FIG. 49A**: B cell depletion in bone marrow of monkeys treated with 5mg/kg 2M24/CD20 hIgG1 KIF or rituximab hIgG1 KIF. **FIG. 49B**: B cell depletion in lymph nodes of monkeys treated with 5mg/kg 2M24/CD20 hIgG1 KIF or rituximab hIgG1 KIF.

[0098] **FIG. 50** shows depletion of B cells from cynomolgus monkey PBMCs *ex vivo*.

[0099] **FIG. 51** shows the format of a bispecific molecule that uses knobs-into-holes technology to pair an anti-CD20 conventional half-antibody with an anti-Dectin-1 single chain variable fragment (scFv) Fc fusion arm (2M24 scFv/CD20). H: 2M24 VH domain; L: 2M24 VL domain.

[0100] **FIGS. 52A-52C** show purification and functional characterization of the 2M24/CD20 bispecific antibody. **FIG. 52A** shows purification of the molecule by size exclusion chromatography (SEC). **FIG. 52B** shows that purified bispecific antibody promoted targeted immune stimulation, as assessed in an

NFκB reporter assay. **FIG. 52C** shows human B cell depletion by the 2M24 scFv/CD20 bispecific antibody.

[0101] **FIGS. 53A-53C** show development and characterization of an anti-Dectin-1 (2M24)/anti-Trop-2 bispecific antibody. **FIG. 53A** shows the purification of 2M24/Trop-2 bispecific antibody by SEC (left). Purified antibody was analyzed by SDS-PAGE under non-reducing (NR) or reducing (R) conditions (right). **FIGS. 53B & 53C** show high affinity binding of the molecule to Dectin-1-expressing HEK cells (**FIG. 53B**) and moderate affinity binding to the Trop-2 expressing A431 cancer cell line (**FIG. 53C**).

[0102] **FIG. 54** shows Trop-2 expression levels on cancer cells.

[0103] **FIGS. 55A-55D** show binding of 2M24/Trop-2 bispecific antibody to Trop-2-expressing cell lines HeLa (**FIG. 55A**), BxPC-3 (**FIG. 55B**), SiHa (**FIG. 55C**), and Capan-2 (**FIG. 55D**). Binding EC50, as determined using four-parameter logistic (4PL) non-linear regression, is shown for each cell line.

[0104] **FIGS. 56A & 56B** show depletion of Trop-2-expressing cell lines (SKBR3 cells in **FIG. 56A**; A431 cells in **FIG. 56B**) using 2M24/Trop-2 bispecific antibody.

[0105] **FIGS. 57A & 57B** show Trop-2 and Dectin-1 expression in a lung cancer biopsy.

[0106] **FIG. 58** shows depletion of Trop-2-positive cancer cells in a lung cancer biopsy.

[0107] **FIG. 59A** shows activity of 2M24/Trop-2 bispecific antibody in an NFκB reporter assay.

[0108] **FIGS. 59B-59E** show that 2M24/Trop-2 bispecific antibody promotes antigen presentation and T cell activation. **FIG. 59B** provides a schematic representation of the assay set up. In **FIG. 59C**, macrophages and SKBR3 breast cancer cells were co-incubated in the presence of 2M24/Trop-2 hIgG1 or control 2M24/RSV hIgG1 bispecific antibody. Phagocytosis or depletion of SKBR3 cells was assessed by flow cytometry by staining for EPCAM expression on SKBR3 cells. Data are reported as relative to the control bispecific 2M24/RSV. In **FIG. 59D**, IFN gamma levels in the supernatants were quantified using the BD OptiEIA Kit. In **FIG. 59E**, expression of CD69, an early activation marker, on T cells was assessed by flow cytometry. Data are reported as relative to total CD3+ T cells.

[0109] **FIGS. 60A & 60B** show design and production of a 2M24/Nectin-4 bispecific antibody. **FIG. 60A** shows a diagram of the bispecific molecule. **FIG. 60B** shows purification of the bispecific antibody using Protein A chromatography.

[0110] **FIGS. 61A & 61B** show Nectin-4 expression on cancer cell lines (**FIG. 61A**) and cancer cells from primary tumor biopsies (**FIG. 61B**).

[0111] **FIG. 62** shows binding of 2M24/Nectin-4 bispecific antibody to Dectin-1-expressing HEK cells (upper) or Nectin-4-expressing A431 cells (lower).

[0112] **FIG. 63** shows stimulation of Dectin-1 in the NFκB reporter assay by 2M24/Nectin-4 bispecific antibody. Upper panel shows a diagram of the assay. Lower panel shows the results, as quantified based on SEAP levels in media.

[0113] **FIGS. 64A & 64B** show depletion of Nectin-4-expressing cancer cells by the 2M24/Nectin-4 bispecific antibody. **FIG. 64A** shows detection of phagocytosis/depletion by flow cytometry. **FIG. 64B** shows depletion relative to RSV control.

[0114] **FIGS. 65A-65C** show that 2M24/11-1F4 bispecific antibody binds to light chain amyloids. **FIG. 65A** shows purification of parental anti-amyloid antibody 11-1F4 (upper) and 2M24/11-1F4 bispecific antibody (lower) by SEC. **FIGS. 65B & 65C** show binding of 11-1F4 parental antibody (**FIG. 65B**) or 2M24/11-1F4 bispecific antibody (**FIG. 65C**) to recombinant light chain amyloids from different patients (AL30, AL47, AL48, and AL55) by Octet.

[0115] **FIG. 66** shows phagocytosis of light chain amyloid fibrils by monocytes.

[0116] **FIG. 67** illustrates the ability to tune the functional activities of a myeloid engager of the present disclosure with an arm that binds Dectin-1 and an arm that binds a target of interest, as well as an Fc region.

[0117] **FIGS. 68A & 68B** show the characterization of 2M24 variants binding to Dectin-1. **FIG. 68A** provides a schematic of the assay used to measure binding via biosensor (Octet). **FIG. 68B** shows variant dissociation rates fitted from biosensor data.

[0118] **FIGS. 69A & 69B** show the effect of modulating Fc region (in this example, KIF-treated hIgG1 vs. hIgG4) on B cell depletion by myeloid cell engagers targeting hDectin-1 (via 2M24) and hCD20 using PBMCs obtained from 2 donors. hIgG4 Fc included S228P mutation (numbering according to EU index).

[0119] **FIGS. 70A-70D** show the effect of modulating Fc region (in this example, mutations that enhance Fc gamma receptor binding) on binding to Fc gamma receptor CD16a F variant by myeloid cell engagers targeting hDectin-1 (via 2M24) using ELISA. Fc mutations used are indicated as follows. SDIE: hIgG1 Fc with S239D and I332E mutations. SDALIE: hIgG1 Fc with S239D, A330L, and I332E mutations. GAALIE: hIgG1 Fc with G236A, S239D, A330L, and I332E mutations. NF: non-fucosylated. All numbering is according to EU index. Fc regions further included knob/hole mutations and RF mutation on one Fc chain for purification (H435R and Y436F in CH3 domain as described by Jendeberg, L. *et al.* (1997, *J. Immunological Meth.*, 201 : 25-34)).

[0120] **FIG. 71** shows how binding affinity for 2M24 variants with alanine substitutions were compared to that of parental antibody using biosensor assays.

[0121] **FIGS. 72A-72C** show characterization of 2M24 variants 2M24.116 and 2M24.119. **FIG. 72A** shows that 2M24 variants in a bispecific antibody with an anti-Trop2 binding arm showed similar potency compared to parental 2M24/Trop2 bispecific in a SEAP reporter assay. **FIG. 72B** shows that 2M24/Trop2, 2M24.116/Trop2, and 2M24.119/Trop2 bispecific antibodies showed similar binding to A431 cells expressing Trop2. EC50 values are shown for each test antibody. **FIG. 72C** shows that 2M24.116 and 2M24.119 showed roughly the same binding to Dectin-1-expressing HEK cells, and that 2M24/Trop2, 2M24.116/Trop2, and 2M24.119/Trop2 bispecific antibodies showed similar binding to Dectin-1-expressing HEK cells. EC50 values are shown for each test antibody.

[0122] **FIG. 73** shows graphical representations of bispecific binding proteins targeting Dectin-1 (*e.g.*, using 2M24 variable domains) and a target of interest comprising disulfide engineering to drive pairing of the correct heavy and light chain variable domains. Shown are traditional bispecific antibody format (left) and a format in which one arm (*i.e.*, the arm binding Dectin-1) is in scFv format (right). Heavy chains are paired with knobs-into-holes mutations. In the Dectin-1 binding arms, cysteines forming native disulfide bonds between heavy and light chains have been removed, and cysteine substitutions have been introduced to give rise to non-native disulfide bonds. The arms binding the target of interest have native disulfide bonds, thereby distinguishing the variable domains for each arm by disulfide bonding position.

[0123] **FIGS. 74A & 74B** show alignments between 2M24 VH domain and CTX-2026 VH domain, and between 2M24 VL domain and CTX-2026 VL domain. Intrachain disulfide bonds are shown in solid lines; interchain disulfide bonds introduced via cysteine substitutions in 2M24 VH and VL domains are shown in dotted lines. **FIG. 74A** shows P1 substitutions; **FIG. 74B** shows P2 substitutions. Sequences depicted correspond to SEQ ID NO:213 for 2M24 P1 VH (2M24_H in **FIG. 74A**), SEQ ID NO:214 for 2M24 P1 VL (2M24_L in **FIG. 74A**), SEQ ID NO:215 for 2M24 P2 VH (2M24_H in **FIG. 74B**), SEQ ID NO:216 for 2M24 P2 VL (2M24_L in **FIG. 74B**), SEQ ID NO:217 for CTX-2026 VH (6XLQ_B in **FIGS. 74A & 74B**), and SEQ ID NO:218 for CTX-2026 VL (6XLQ_C in **FIGS. 74A & 74B**).

[0124] **FIG. 75A** shows results of a SEAP secretion assay using hDectin-1-expressing HEK cells with the SEAP Dectin-1 reporter and Raji cells (expressing CD20). Bispecific antibodies targeting Dectin-1 and CD20 were assayed, using DuetMab subsitutions to drive heavy/light chain pairing (Duet), 2M24 P1 VH and VL domains (hG1 SS P1), 2M24 P2 VH and VL domains (hG1 SS P2), control 2M24/RSV bispecific, and control 2M24 antibody. OD_{630} based on the SEAP reporter of the hDectin-1-expressing HEK cells was tracked as a function of antibody concentration.

[0125] **FIG. 75B** shows results of B cell depletion assays using healthy donor PBMCs from 2 donors (left and right). Ability of a bispecific antibody with 2M24 P1 VH and VL domains in one arm and anti-CD20 binding domains in the other (active hIgG1 Fc) to deplete B cells was compared against isotype control RSV antibody. Plots show the levels of remaining live, CD19+ B cells (reported as a % of B cells in isotype control-treated PBMCs) vs. concentration of antibody after 24 hour incubation.

[0126] **FIG. 76A** shows protein A purification of 2M24/CD20 bispecific binding proteins in which 2M24 arm was in scFv format (formats are shown at right). Bispecific binding protein with parental 2M24 scFv were compared to bispecific binding protein with 2M24 P1 variant scFv. Percentage of each species purified as oligomers vs. monomer are depicted for each binding protein. 60-70% of parental 2M24 scFv/CD20 bispecific was in monomeric form, compared to over 96% of 2M24 P1 variant scFv/CD20 bispecific, indicating that the disulfide variant was more stable/less prone to oligomerization during protein A affinity purification.

[0127] **FIG. 76B** shows binding of 2M24/CD20 bispecific binding proteins to HEK cells expressing hDectin-1 (upper) or to Raji cells expressing CD20 (lower), compared to secondary antibody only. A4: 2M24 parental VH and VL domains. A37: 2M24 P1 variant VH and VL domains.

[0128] **FIG. 76C** shows activity of 2M24/CD20 bispecific binding proteins in a SEAP reporter assay with hDectin-1-expressing HEK cells bearing the SEAP Dectin-1 reporter and Raji cells (expressing CD20) at 1:1 ratio. A4: 2M24 parental VH and VL domains. A37: 2M24 P1 variant VH and VL domains. B01: mIgG2a negative control.

[0129] **FIG. 76D** compares ability of 2M24/CD20 bispecific binding proteins in which 2M24 arm was in scFv format (either parental 2M24 or P1 variant 2M24 variable domains) to deplete B cells from human PBMCs from 2 healthy donors (left and right), as compared to isotype control.

[0130] **FIG. 76E** shows abundance of oligomer vs. monomer from protein A purification for 2M24/CD20 bispecific binding proteins in which 2M24 arm was in scFv format (parental 2M24) after 1 week at 5°C or 25°C (upper left), or 2M24/CD20 bispecific binding proteins in which 2M24 arm was in scFv format (P1 variant 2M24) after 4 weeks at 5°C or 25°C (upper right). Stability (depicted as % monomer species) over time is shown for parental 2M24 and P1 variant 2M24 at 5°C and 25°C (lower).

[0131] **FIG. 77** shows B cell depletion (%CD19+ of CD45+ cells) from human PBMCs from 2 healthy donors (left and right) vs. antibody concentration after 24 hour incubation for 2M24/CD20 bispecific binding proteins having human IgG4, human IgG1, or non-fucosylated human IgG1 Fc region, compared to isotype control.

DETAILED DESCRIPTION

[0132] Several aspects are described below with reference to example applications for illustration. It should be understood that numerous specific details, relationships, and methods are set forth to provide a full understanding of the features described herein. One having ordinary skill in the relevant art, however, will readily recognize that the features described herein can be practiced without one or more of the specific details or with other methods. The features described herein are not limited by the illustrated ordering of acts or events, as some acts can occur in different orders and/or concurrently with other acts or events. Furthermore, not all illustrated acts or events are required to implement a methodology in accordance with the features described herein.

[0133] As used herein, the singular forms "a", "an", and "the" are intended to include the plural forms as well, unless the context clearly indicates otherwise. Furthermore, to the extent that the terms "including", "includes", "having", "has", "with", or variants thereof are used in either the detailed description and/or the claims, such terms are intended to be inclusive in a manner similar to the term "comprising". The term "comprising" as used herein is synonymous with "including" or "containing", and is inclusive or open-ended.

[0134] Any reference to "or" herein is intended to encompass "and/or" unless otherwise stated. As used herein, the term "about" with reference to a number refers to that number plus or minus 10% of that number. The term "about" with reference to a range refers to that range minus 10% of its lowest value and plus 10% of its greatest value.

I. Antibodies and Multispecific Binding Proteins

[0135] In certain aspects, the present disclosure provides antigen binding domains, antibodies, and antibody fragments that bind to human Dectin-1, as well as multispecific (*e.g.*, bispecific) binding molecules comprising the same. In some embodiments, provided herein are the anti-Dectin-1 antigen binding domain 2M24, which is described in International Appl. No. PCT/US2021/071752, filed Oct. 6, 2021, and variants thereof.

[0136] In some embodiments, antibody and immunoglobulin are used interchangeably and herein are used in the broadest sense and encompass various antibody structures, including but not limited to monoclonal antibodies (e.g., full length or intact monoclonal antibodies), polyclonal antibodies, multispecific antibodies (e.g., bispecific antibodies), antibody fragments and single domain antibody (as described in greater detail herein), so long as they exhibit the desired antigen binding activity.

[0137] In some embodiments, antibodies (immunoglobulins) refer to a protein having a structure substantially similar to a native antibody structure, or a protein having heavy and light chain variable regions having structures substantially similar to native heavy and light chain variable region structures. Native antibodies refer to naturally occurring immunoglobulin molecules with varying structures. For example, native immunoglobulins of the IgG class are heterotetrameric glycoproteins of about 150,000 daltons, composed of two light chains and two heavy chains that are disulfide-bonded. From N- to C-terminus, each heavy chain has a variable region (VH), also called a variable heavy domain or a heavy chain variable domain, followed by three constant domains (CH1, CH2, and CH3), also called a heavy chain constant region. Similarly, from N- to C-terminus, each light chain has a variable region (VL), also called a variable light domain or a light chain variable domain, followed by a constant light (CL) domain, also called a light chain constant region. The subunit structures and three-dimensional configurations of the different classes of immunoglobulins are well known and described generally, for example, in Abbas et al., 2000, Cellular and Mol, and Kindt et al., Kuby Immunology, 6th ed., W.H. Freeman and Co., page 91 (2007). Antibodies (immunoglobulins) are assigned to different classes, depending on the amino acid sequences of the heavy chain constant domains. There are five major classes of antibodies: α (IgA), δ (IgD), ϵ (IgE), γ (IgG), or μ (IgM), some of which may be further divided into subtypes, e.g., γ1 (IgG1), γ2 (IgG2), γ3 (IgG3), γ4 (IgG4), α1 (IgA1) and α2 (IgA2). The light chain of an immunoglobulin may be assigned to one of two types, called kappa (κ) and lambda (λ), based on the amino acid sequence of its constant domain. An immunoglobulin essentially consists of two Fab molecules and an Fc domain, linked via the immunoglobulin hinge region.

[0138] In some embodiments, an Fc, Fc region, or Fc domain refers to the C-terminal region of an antibody heavy chain that contains at least a portion of the constant region. The term includes native sequence Fc regions and variant Fc regions. An Fc can refer to the last two constant region immunoglobulin domains (e.g., CH2 and CH3) of IgA, IgD, and IgG, the last three constant region immunoglobulin domains of IgE and IgM, and optionally, all or a portion of the flexible hinge N-terminal to these domains. For IgA and IgM, Fc may include the J chain. An IgG Fc region comprises an IgG CH2

and an IgG CH3 domain and in some cases, inclusive of the hinge. Unless otherwise specified herein, numbering of amino acid residues in the Fc region or constant region is according to the EU numbering system, also called the EU index, as described in Kabat et al., Sequences of Proteins of Immunological Interest, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, Md., 1991. Human IgG Fc domains are of particular use in the present disclosure, and can be the Fc domain from human IgG1, IgG2 or IgG4.

[0139] As is known in the art, variable domains of the heavy chain and light chain (VH and VL, respectively) of an antibody generally have similar structures, with each domain comprising four conserved framework regions (FRs) and three complementarity-determining regions (CDRs). (See, e.g., Kindt et al. *Kuby Immunology*, 6th ed., W.H. Freeman and Co., page 91 (2007).) Framework (or "FR" as used herein) can refer to variable domain residues other than the CDR residues. The FR of a variable domain generally consists of four FR domains: FR1, FR2, FR3, and FR4. Accordingly, the CDR and FR sequences generally appear in the following sequence in VH (or VL): FR1-CDR1-FR2-CDR2-FR3-CDR3-FR4. In some embodiments, a FR1, FR2, FR3, and/or FR4 of the present disclosure refers to a human framework region, *i.e.*, of the VH or VL domain.

[0140] In some embodiments, the antigen binding domain, antibody, or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises the amino acid sequence QVQLVQSGAEVKKPGASVKVSCKSSGYTFTX$_1$YYIHWVRQAPGQGLEWMGWINPNSGX$_2$TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCAX$_3$X$_4$X$_5$X$_6$X$_7$X$_8$X$_9$X$_{10}$X$_{11}$X$_{12}$WGQGTLVTVSS, wherein X$_1$ is D, A, or G; wherein X$_2$ is D, A, or G; wherein X$_3$ is R, A, or G; wherein X$_4$ is N, A, or G; wherein X$_5$ is S, A, or G; wherein X$_6$ is A or G; wherein X$_7$ is S, A, or G; wherein X$_8$ is Y, A, or G; wherein X$_9$ is S, A, or G; wherein X$_{10}$ is F, A, or G; wherein X$_{11}$ is A or G; and wherein X$_{12}$ is Y, A, or G (SEQ ID NO:63); and wherein the VL domain comprises the amino acid sequence DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPSRFSGSGSGTDFTLTVSSLQPEDFATYYCX$_1$X$_2$AX$_3$X$_4$X$_5$X$_6$X$_7$X$_8$FGPGTKVDIE, wherein X$_1$ is Q, A, or G; X$_2$ is Q, A, or G; X$_3$ is F, Y, A, or G; wherein X$_4$ is S, A, or G; wherein X$_5$ is F, A, or G; wherein X$_6$ is P, A, or G; wherein X$_7$ is F, A, or G; and wherein X$_8$ is T, A, or G (SEQ ID NO:65). In some embodiments, the antigen binding domain, antibody, or fragment does not comprise a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3), a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the VH domain comprises 1, 2 or fewer, 3 or fewer, 4 or fewer, or 5 or fewer substitutions as compared to the amino acid sequence of SEQ ID NO:62; and/or wherein the VL domain comprises 1, 2 or fewer, 3 or fewer, 4 or fewer, or 5 or fewer substitutions as compared to the amino acid sequence of SEQ ID NO:64.

In some embodiments, the antigen binding domain, antibody, or fragment binds to human Dectin-1 expressed on the surface of a cell with an EC50 of less than 2nM; is capable of binding human or cynomolgus Dectin-1; and/or does not compete with a native ligand of human Dectin-1.

[0141] In some embodiments, the antigen binding domain, antibody, or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises: a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1) or AYYI (SEQ ID NO: 16); a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2) or WINPNSGATNYAQKFQG (SEQ ID NO: 19); and a CDR-H3 comprising an amino acid sequence selected from the group consisting of NSGSYSFGY (SEQ ID NO: 3), ASGSYSFGY (SEQ ID NO: 22), NSGSASFGY (SEQ ID NO: 24), NAGSYSFGY (SEQ ID NO: 27), NSASYSFGY (SEQ ID NO: 29), NSGAYSFGY (SEQ ID NO: 31), NSGSYAFGY (SEQ ID NO: 33), NSGSYSAGY (SEQ ID NO: 35), NSGSYSFAY (SEQ ID NO: 37), and NSGSYSFGA (SEQ ID NO: 39); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4); a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising an amino acid sequence selected from the group consisting of QQAYSFPFT (SEQ ID NO: 6), QQAASFPFT (SEQ ID NO: 41), QQAFSFPFT (SEQ ID NO: 42), AQAYSFPFT (SEQ ID NO: 43), QAAYSFPFT (SEQ ID NO: 44), QQAYAFPFT (SEQ ID NO: 45), QQAYSAPFT (SEQ ID NO: 46), QQAYSFAFT (SEQ ID NO: 47), QQAYSFPAT (SEQ ID NO: 48), and QQAYSFPFA (SEQ ID NO: 49). In some embodiments, the antigen binding domain, antibody, or fragment does not comprise a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3), a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence AYYI (SEQ ID NO: 16), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGATNYAQKFQG (SEQ ID NO: 19), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence ASGSYSFGY (SEQ ID NO: 22). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2

comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSASFGY (SEQ ID NO: 24). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NAGSYSFGY (SEQ ID NO: 27). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSASYSFGY (SEQ ID NO: 29). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGAYSFGY (SEQ ID NO: 31). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYAFGY (SEQ ID NO: 33). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSAGY (SEQ ID NO: 35). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSFAY (SEQ ID NO: 37). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSFGA (SEQ ID NO: 39). In some embodiments, the VH domain further comprises a FR1 comprising an amino acid sequence selected from the group consisting of QVQLVQSGAEVKKPGASVKVSCKSSGYTFT (SEQ ID NO:50) and QVQLVQSGAEVKKPGASVKVSCKASGYTFT (SEQ ID NO:51); a FR2 comprising the amino acid sequence HWVRQAPGQGLEWMG (SEQ ID NO:52); a FR3 comprising an amino acid sequence selected from the group consisting of RITMTRDTSISTAYLELSRLRSDDTAVFYCAR (SEQ ID NO:53) and RVTMTRDTSISTAYMELSRLRSDDTAVYYCAR (SEQ ID NO:54); and a FR4 comprising the amino acid sequence WGQGTLVTVSS (SEQ ID NO:55). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAASFPFT (SEQ ID NO: 41). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino

acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAFSFPFT (SEQ ID NO: 42). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence AQAYSFPFT (SEQ ID NO: 43). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QAAYSFPFT (SEQ ID NO: 44). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYAFPFT (SEQ ID NO: 45). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSAPFT (SEQ ID NO: 46). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFAFT (SEQ ID NO: 47). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPAT (SEQ ID NO: 48). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFA (SEQ ID NO: 49). In some embodiments, the VL domain further comprises a FR1 comprising the amino acid sequence DIQMTQSPSSVSASVGDRVTITC (SEQ ID NO:56); a FR2 comprising an amino acid sequence selected from the group consisting of WYQQKPGKAPKLLIF (SEQ ID NO:57) and WYQQKPGKAPKLLIY (SEQ ID NO:58); a FR3 comprising an amino acid sequence selected from the group consisting of GVPSRFSGSGSGTDFTLTVSSLQPEDFATYYC (SEQ ID NO:59) and GVPSRFSGSGSGTDFTLTISSLQPEDFATYYC (SEQ ID NO:60); and a FR4 comprising the amino acid sequence FGPGTKVDIE (SEQ ID NO:61).

[0142] Multiple definitions for the CDR sequences of antibody variable domains are known in the art; *see, e.g.*, Kabat (*Sequences of Proteins of Immunological Interest*, Fifth Edition, NIH Publication 91-3242, Bethesda MD (1991), vols. 1-3) and Chothia. Unless otherwise specified, CDR sequences are described herein according to the definition of IMGT. *See, e.g.*, www.imgt.org/IMGTScientificChart/Nomenclature/IMGT-FRCDRdefinition.html.

[0143] In some embodiments, the antigen binding domain, antibody, or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises: a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7) or GYTFTAYY (SEQ ID

NO:17); a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8) or INPNSGAT (SEQ ID NO: 20); and a CDR-H3 comprising an amino acid sequence selected from the group consisting of ARNSGSYSFGY (SEQ ID NO: 9), ARASGSYSFGY (SEQ ID NO: 23), ARNSGSASFGY (SEQ ID NO: 25), AANSGSYSFGY (SEQ ID NO: 26), ARNAGSYSFGY (SEQ ID NO: 28), ARNSASYSFGY (SEQ ID NO: 30), ARNSGAYSFGY (SEQ ID NO: 32), ARNSGSYAFGY (SEQ ID NO: 34), ARNSGSYSAGY (SEQ ID NO: 36), ARNSGSYSFAY (SEQ ID NO: 38), and ARNSGSYSFGA (SEQ ID NO: 40); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10); a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising an amino acid sequence selected from the group consisting of QQAYSFPFT (SEQ ID NO: 12), QQAASFPFT (SEQ ID NO: 41), QQAFSFPFT (SEQ ID NO: 42), AQAYSFPFT (SEQ ID NO: 43), QAAYSFPFT (SEQ ID NO: 44), QQAYAFPFT (SEQ ID NO: 45), QQAYSAPFT (SEQ ID NO: 46), QQAYSFAFT (SEQ ID NO: 47), QQAYSFPAT (SEQ ID NO: 48), and QQAYSFPFA (SEQ ID NO: 49). In some embodiments, the antigen binding domain, antibody, or fragment does not comprise a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), a CDR-H3 comprising the amino acid sequence ARNSGSYSFGY (SEQ ID NO: 9), a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 12). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARNSGSYSFGY (SEQ ID NO: 9). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTAYY (SEQ ID NO:17), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARNSGSYSFGY (SEQ ID NO: 9). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGAT (SEQ ID NO: 20), and a CDR-H3 comprising the amino acid sequence ARNSGSYSFGY (SEQ ID NO: 9). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARASGSYSFGY (SEQ ID NO: 23). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARNSGSASFGY (SEQ ID NO: 25). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence AANSGSYSFGY (SEQ ID NO: 26). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid

sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARNAGSYSFGY (SEQ ID NO: 28). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARNSASYSFGY (SEQ ID NO: 30). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARNSGAYSFGY (SEQ ID NO: 32). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARNSGSYAFGY (SEQ ID NO: 34). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARNSGSYSAGY (SEQ ID NO: 36). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARNSGSYSFAY (SEQ ID NO: 38). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARNSGSYSFGA (SEQ ID NO: 40). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 12). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence QQAASFPFT (SEQ ID NO: 41). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence QQAFSFPFT (SEQ ID NO: 42). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence AQAYSFPFT (SEQ ID NO: 43). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence QAAYSFPFT (SEQ ID NO: 44). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence QQAYAFPFT (SEQ ID NO: 45). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence QGISSW (SEQ

ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence QQAYSAPFT (SEQ ID NO: 46). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence QQAYSFAFT (SEQ ID NO: 47). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence QQAYSFPAT (SEQ ID NO: 48). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence QQAYSFPFA (SEQ ID NO: 49).

[0144] In some embodiments, the antigen binding domain, antibody, or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises: a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13) or GYTFTAY (SEQ ID NO:18); a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14) or NPNSGA (SEQ ID NO: 21); and a CDR-H3 comprising an amino acid sequence selected from the group consisting of NSGSYSFGY (SEQ ID NO: 15), ASGSYSFGY (SEQ ID NO: 22), NSGSASFGY (SEQ ID NO: 24), NAGSYSFGY (SEQ ID NO: 27), NSASYSFGY (SEQ ID NO: 29), NSGAYSFGY (SEQ ID NO: 31), NSGSYAFGY (SEQ ID NO: 33), NSGSYSAGY (SEQ ID NO: 35), NSGSYSFAY (SEQ ID NO: 37), and NSGSYSFGA (SEQ ID NO: 39); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4); a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising an amino acid sequence selected from the group consisting of QQAYSFPFT (SEQ ID NO: 6), QQAASFPFT (SEQ ID NO: 41), QQAFSFPFT (SEQ ID NO: 42), AQAYSFPFT (SEQ ID NO: 43), QAAYSFPFT (SEQ ID NO: 44), QQAYAFPFT (SEQ ID NO: 45), QQAYSAPFT (SEQ ID NO: 46), QQAYSFAFT (SEQ ID NO: 47), QQAYSFPAT (SEQ ID NO: 48), and QQAYSFPFA (SEQ ID NO: 49). In some embodiments, the antibody does not comprise a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 15), a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 15). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTAY (SEQ ID NO:18), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 15). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid

sequence NPNSGA (SEQ ID NO: 21), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 15). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence ASGSYSFGY (SEQ ID NO: 22). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence NAGSYSFGY (SEQ ID NO: 27). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence NSASYSFGY (SEQ ID NO: 29). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence NSGAYSFGY (SEQ ID NO: 31). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence NSGSYAFGY (SEQ ID NO: 33). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence NSGSYSAGY (SEQ ID NO: 35). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence NSGSYSFAY (SEQ ID NO: 37). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence NSGSYSFGA (SEQ ID NO: 39). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAASFPFT (SEQ ID NO: 41). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAFSFPFT (SEQ ID NO: 42). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence AQAYSFPFT (SEQ ID NO: 43). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence

RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QAAYSFPFT (SEQ ID NO: 44). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYAFPFT (SEQ ID NO: 45). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSAPFT (SEQ ID NO: 46). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFAFT (SEQ ID NO: 47). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPAT (SEQ ID NO: 48). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFA (SEQ ID NO: 49).

[0145] In some embodiments, the VH domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos:62 and 82-93. In some embodiments, In some embodiments according to any of the embodiments described herein, the VL domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos: 64 and 94-102. In some embodiments, the VH domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos:62 and 82-93 and/or the VL domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos: 64 and 94-102. In some embodiments, the antibody does not comprise a VH domain comprising the amino acid sequence of SEQ ID NO:62 and a VL domain comprising the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain comprises

the amino acid sequence of SEQ ID NO:62, and the VL domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:82, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:82, and the VL domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:83, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:83, and the VL domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:84, and the VL domain

comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:84, and the VL domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:85, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:85, and the VL domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:86, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:86, and the VL domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain comprises the amino acid sequence of SEQ ID NO:95. In some

embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:87, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:87, and the VL domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:88, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:88, and the VL domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID

NO: 88, and the VL domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:89, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:89, and the VL domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:90, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:90, and the VL domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain comprises the amino acid sequence of

SEQ ID NO:100. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:91, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:91, and the VL domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:92, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:92, and the VL domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain comprises the amino acid sequence of SEQ ID NO:102. In some embodiments, the VH domain comprises

the amino acid sequence of SEQ ID NO:93, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:93, and the VL domain comprises the amino acid sequence of SEQ ID NO:94. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain comprises the amino acid sequence of SEQ ID NO:95. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain comprises the amino acid sequence of SEQ ID NO:96. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain comprises the amino acid sequence of SEQ ID NO:97. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain comprises the amino acid sequence of SEQ ID NO:98. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain comprises the amino acid sequence of SEQ ID NO:99. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain comprises the amino acid sequence of SEQ ID NO:100. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain comprises the amino acid sequence of SEQ ID NO:101. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain comprises the amino acid sequence of SEQ ID NO:102.

[0146] In some embodiments, the antigen binding domain, antibody, or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises the amino acid sequence QVQLVQSGAEVKKPGASVKVSCKX$_1$SGYTFTX$_2$YYX$_3$HWVRQAPGQGLEWMGWINPNSGX$_4$TNYAQKFQGRX$_5$TMTRDTSISTAYX$_6$ELSRLRSDDTAVX$_7$YCARNSGSYSFGYWGQGTLVTVSS; wherein X$_1$ is S or A; wherein X$_2$ is D or G; wherein X$_3$ is I or M; wherein X$_4$ is D or G; wherein X$_5$ is I or V; wherein X$_6$ is L or M; and wherein X$_7$ is F or Y (SEQ ID NO:80); and wherein the VL domain comprises the amino acid sequence DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIX$_1$X$_2$ASSLQSGVPSRFSGSGSGTDFTLTX$_3$SSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE; wherein X$_1$ is F or Y; wherein X$_2$ is G or A; and wherein X$_3$ is V or I (SEQ ID NO:81). In some embodiments, the antigen binding domain, antibody, or fragment does not comprise a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3), a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6).

[0147] In some embodiments, the antigen binding domain, antibody, or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises: a CDR-H1 comprising an amino acid sequence selected from the group consisting of DYYI (SEQ ID NO: 1), DYYM (SEQ ID NO: 66), and GYYM (SEQ ID NO: 67); a CDR-H2 comprising the amino acid

sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2) or WINPNSGGTNYAQKFQG (SEQ ID NO: 70); and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4); a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5) or AASSLQS (SEQ ID NO: 73), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the antigen binding domain, antibody, or fragment does not comprise a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3), a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence DYYM (SEQ ID NO: 66), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYYM (SEQ ID NO: 67), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence DYYM (SEQ ID NO: 66), a CDR-H2 comprising the amino acid sequence WINPNSGGTNYAQKFQG (SEQ ID NO: 70), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYYM (SEQ ID NO: 67), a CDR-H2 comprising the amino acid sequence WINPNSGGTNYAQKFQG (SEQ ID NO: 70), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3). In some embodiments, the VH domain further comprises a FR1 comprising an amino acid sequence selected from the group consisting of QVQLVQSGAEVKKPGASVKVSCKSSGYTFT (SEQ ID NO:50) and QVQLVQSGAEVKKPGASVKVSCKASGYTFT (SEQ ID NO:76); a FR2 comprising the amino acid sequence HWVRQAPGQGLEWMG (SEQ ID NO:52); a FR3 comprising an amino acid sequence selected from the group consisting of RITMTRDTSISTAYLELSRLRSDDTAVFYCAR (SEQ ID NO:53) and RVTMTRDTSISTAYMELSRLRSDDTAVYYCAR (SEQ ID NO:77); and a FR4 comprising the amino acid sequence WGQGTLVTVSS (SEQ ID NO:55). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the

amino acid sequence AASSLQS (SEQ ID NO: 73), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the VL domain further comprises a FR1 comprising the amino acid sequence DIQMTQSPSSVSASVGDRVTITC (SEQ ID NO:56); a FR2 comprising an amino acid sequence selected from the group consisting of WYQQKPGKAPKLLIF (SEQ ID NO:57) and WYQQKPGKAPKLLIY (SEQ ID NO:78); a FR3 comprising an amino acid sequence selected from the group consisting of GVPSRFSGSGSGTDFTLTVSSLQPEDFATYYC (SEQ ID NO:59) and GVPSRFSGSGSGTDFTLTISSLQPEDFATYYC (SEQ ID NO:79); and a FR4 comprising the amino acid sequence FGPGTKVDIE (SEQ ID NO:61).

[0148] In some embodiments, the antigen binding domain, antibody, or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises: a CDR-H1 comprising an amino acid sequence selected from the group consisting of GYTFTDYY (SEQ ID NO:7), and GYTFTGYY (SEQ ID NO:68); a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8) or INPNSGGT (SEQ ID NO:71); and a CDR-H3 comprising the amino acid sequence ARNSGSYSFGY (SEQ ID NO: 9); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10); a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11) or AAS (SEQ ID NO: 74), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 12). In some embodiments, the antigen binding domain, antibody, or fragment does not comprise a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), a CDR-H3 comprising the amino acid sequence ARNSGSYSFGY (SEQ ID NO: 9), a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 12). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARNSGSYSFGY (SEQ ID NO: 9). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTGYY (SEQ ID NO:68), a CDR-H2 comprising the amino acid sequence INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence ARNSGSYSFGY (SEQ ID NO: 9). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence INPNSGGT (SEQ ID NO:71), and a CDR-H3 comprising the amino acid sequence ARNSGSYSFGY (SEQ ID NO: 9). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTGYY (SEQ ID NO:68), a CDR-H2 comprising the amino acid sequence INPNSGGT (SEQ ID NO:71), and a CDR-H3 comprising the amino acid sequence ARNSGSYSFGY (SEQ ID NO: 9). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 12). In some embodiments, the VL domain comprises a CDR-L1

comprising the amino acid sequence QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence AAS (SEQ ID NO: 74), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 12).

[0149] In some embodiments, the antigen binding domain, antibody, or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises: a CDR-H1 comprising an amino acid sequence selected from the group consisting of GYTFTDY (SEQ ID NO:13), and GYTFTGY (SEQ ID NO:69); a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14) or NPNSGG (SEQ ID NO: 72); and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 15); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4); a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5) or AASSLQS (SEQ ID NO: 75), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the antigen binding domain, antibody, or fragment does not comprise a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 15), a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 15). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTGY (SEQ ID NO:69), a CDR-H2 comprising the amino acid sequence NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 15). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence NPNSGG (SEQ ID NO: 72), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 15). In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence GYTFTGY (SEQ ID NO:69), a CDR-H2 comprising the amino acid sequence NPNSGG (SEQ ID NO: 72), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 15). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the VL domain comprises a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence AASSLQS (SEQ ID NO: 75), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6).

[0150] In some embodiments, the VH domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos: 62 and 103-109. In some embodiments, the VL domain comprises an

amino acid sequence selected from the group consisting of SEQ ID Nos:64 and 110-113. In some embodiments, the VH domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos: 62 and 103-109 and/or the VL domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos:64 and 110-113. In some embodiments, the antibody does not comprise a VH domain comprising the amino acid sequence of SEQ ID NO:62 and a VL domain comprising the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 62, and the VL domain comprises the amino acid sequence of SEQ ID NO:110. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 62, and the VL domain comprises the amino acid sequence of SEQ ID NO:111. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 62, and the VL domain comprises the amino acid sequence of SEQ ID NO:112. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 62, and the VL domain comprises the amino acid sequence of SEQ ID NO:113. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 103, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 103, and the VL domain comprises the amino acid sequence of SEQ ID NO:110. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 103, and the VL domain comprises the amino acid sequence of SEQ ID NO:111. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 103, and the VL domain comprises the amino acid sequence of SEQ ID NO:112. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 103, and the VL domain comprises the amino acid sequence of SEQ ID NO:113. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 104, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 104, and the VL domain comprises the amino acid sequence of SEQ ID NO:110. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 104, and the VL domain comprises the amino acid sequence of SEQ ID NO:111. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 104, and the VL domain comprises the amino acid sequence of SEQ ID NO:112. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 104, and the VL domain comprises the amino acid sequence of SEQ ID NO:113. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 105, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 105, and the VL domain comprises the amino acid sequence of SEQ ID NO:110. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 105, and the VL domain comprises the amino acid sequence of SEQ ID NO:111. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 105, and the VL domain comprises the amino acid sequence of SEQ ID NO:112. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 105, and the VL domain comprises the amino acid sequence of SEQ ID NO:113. In some

embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 106, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 106, and the VL domain comprises the amino acid sequence of SEQ ID NO:110. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 106, and the VL domain comprises the amino acid sequence of SEQ ID NO:111. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 106, and the VL domain comprises the amino acid sequence of SEQ ID NO:112. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 106, and the VL domain comprises the amino acid sequence of SEQ ID NO:113. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 107, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 107, and the VL domain comprises the amino acid sequence of SEQ ID NO:110. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 107, and the VL domain comprises the amino acid sequence of SEQ ID NO:111. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 107, and the VL domain comprises the amino acid sequence of SEQ ID NO:112. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 107, and the VL domain comprises the amino acid sequence of SEQ ID NO:113. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 108, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 108, and the VL domain comprises the amino acid sequence of SEQ ID NO:110. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 108, and the VL domain comprises the amino acid sequence of SEQ ID NO:111. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 108, and the VL domain comprises the amino acid sequence of SEQ ID NO:112. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 108, and the VL domain comprises the amino acid sequence of SEQ ID NO:113. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 109, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 109, and the VL domain comprises the amino acid sequence of SEQ ID NO:110. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 109, and the VL domain comprises the amino acid sequence of SEQ ID NO:111. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 109, and the VL domain comprises the amino acid sequence of SEQ ID NO:112. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 109, and the VL domain comprises the amino acid sequence of SEQ ID NO:11.

[0151] In some embodiments, an antigen binding domain, antibody, or fragment of the disclosure comprises a VH domain comprising 1, 2, or 3 CDRs from a single VH domain listed in Table 5 and/or a VL domain comprising 1, 2, or 3 CDRs from a single VL domain listed in Table 5. In some

embodiments, an antigen binding domain, antibody, or fragment of the disclosure comprises a VH domain comprising 1, 2, or 3 CDRs from a single VH domain listed in Table 6 and/or a VL domain comprising 1, 2, or 3 CDRs from a single VL domain listed in Table 6. In some embodiments, an antigen binding domain, antibody, or fragment of the disclosure comprises a VH and/or VL domain listed in Table 6. As illustrated below and described herein, in some embodiments, any set of 3 VH CDRs shown in Table 5 can be combined with any set of 3 VL CDRs shown in Table 5 in an antigen binding domain, antibody, or fragment of the present disclosure. In some embodiments, any set of 3 CDRs from a VH domain shown in Table 6 can be combined with any set of 3 CDRs from a VL domain shown in Table 6 in an antigen binding domain, antibody, or fragment of the present disclosure. In some embodiments, any VH domain shown in Table 6 can be combined with any VL domain shown in Table 6 in an antigen binding domain, antibody, or fragment of the present disclosure.

Table 5. Anti-Dectin-1 antibody CDR sequences

Name	*CDR-H1*	*CDR-H2*	*CDR-H3*	*CDR-L1*	*CDR-L2*	*CDR-L3*
2M24 (Kabat)	DYYI (SEQ ID NO: 1)	WINPNSG DTNYAQ KFQG (SEQ ID NO: 2)	NSGSYSFG Y (SEQ ID NO: 3)	RASQGIS SWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYSFPFT (SEQ ID NO: 6)
2M24 (IMGT)	GYTFTDY Y (SEQ ID NO:7)	INPNSGD T (SEQ ID NO: 8)	ARNSGSYS FGY (SEQ ID NO: 9)	QGISSW (SEQ ID NO: 10)	GAS (SEQ ID NO: 11)	QQAYSFPFT (SEQ ID NO: 12)
2M24 (Chothia)	GYTFTDY (SEQ ID NO:13)	NPNSGD (SEQ ID NO: 14)	NSGSYSFG Y (SEQ ID NO: 15)	RASQGIS SWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYSFPFT (SEQ ID NO: 6)
2M24A.1. 11 (Kabat)	AYYI (SEQ ID NO: 16)	WINPNSG DTNYAQ KFQG (SEQ ID NO: 2)	NSGSYSFG Y (SEQ ID NO: 3)			
2M24A.1. 11 (IMGT)	GYTFTAY Y (SEQ ID NO:17)	INPNSGD T (SEQ ID NO: 8)	ARNSGSYS FGY (SEQ ID NO: 9)			
2M24A.1. 11 (Chothia)	GYTFTAY (SEQ ID NO:18)	NPNSGD (SEQ ID NO: 14)	NSGSYSFG Y (SEQ ID NO: 15)			
2M24A.1. 12 (Kabat)	DYYI (SEQ ID NO: 1)	WINPNSG ATNYAQ KFQG (SEQ ID NO: 19)	NSGSYSFG Y (SEQ ID NO: 3)			
2M24A.1. 12 (IMGT)	GYTFTDY Y (SEQ ID NO:7)	INPNSGA T (SEQ ID NO: 20)	ARNSGSYS FGY (SEQ ID NO: 9)			

2M24A.1.12 (Chothia)	GYTFTDY (SEQ ID NO:13)	NPNSGA (SEQ ID NO: 21)	NSGSYSFGY (SEQ ID NO: 15)			
2M24A.1.13 (Kabat)	DYYI (SEQ ID NO: 1)	WINPNSGDTNYAQKFQG (SEQ ID NO: 2)	ASGSYSFGY (SEQ ID NO: 22)			
2M24A.1.13 (IMGT)	GYTFTDYY (SEQ ID NO:7)	INPNSGDT (SEQ ID NO: 8)	ARASGSYSFGY (SEQ ID NO: 23)			
2M24A.1.13 (Chothia)	GYTFTDY (SEQ ID NO:13)	NPNSGD (SEQ ID NO: 14)	ASGSYSFGY (SEQ ID NO: 22)			
2M24A.1.14 (Kabat)	DYYI (SEQ ID NO: 1)	WINPNSGDTNYAQKFQG (SEQ ID NO: 2)	NSGSASFGY (SEQ ID NO: 24)			
2M24A.1.14 (IMGT)	GYTFTDYY (SEQ ID NO:7)	INPNSGDT (SEQ ID NO: 8)	ARNSGSASFGY (SEQ ID NO: 25)			
2M24A.1.14 (Chothia)	GYTFTDY (SEQ ID NO:13)	NPNSGD (SEQ ID NO: 14)	NSGSASFGY (SEQ ID NO: 24)			
2M24A.1.15 (Kabat)	DYYI (SEQ ID NO: 1)	WINPNSGDTNYAQKFQG (SEQ ID NO: 2)	NSGSYSFGY (SEQ ID NO: 3)			
2M24A.1.15 (IMGT)	GYTFTDYY (SEQ ID NO:7)	INPNSGDT (SEQ ID NO: 8)	AANSGSYSFGY (SEQ ID NO: 26)			
2M24A.1.15 (Chothia)	GYTFTDY (SEQ ID NO:13)	NPNSGD (SEQ ID NO: 14)	NSGSYSFGY (SEQ ID NO: 15)			
2M24A.1.16 (Kabat)	DYYI (SEQ ID NO: 1)	WINPNSGDTNYAQKFQG (SEQ ID NO: 2)	NAGSYSFGY (SEQ ID NO: 27)			
2M24A.1.16 (IMGT)	GYTFTDYY (SEQ ID NO:7)	INPNSGDT (SEQ ID NO: 8)	ARNAGSYSFGY (SEQ ID NO: 28)			
2M24A.1.16 (Chothia)	GYTFTDY (SEQ ID NO:13)	NPNSGD (SEQ ID NO: 14)	NAGSYSFGY (SEQ ID NO: 27)			
2M24A.1.17 (Kabat)	DYYI (SEQ ID NO: 1)	WINPNSGDTNYAQKFQG (SEQ ID NO: 2)	NSASYSFGY (SEQ ID NO: 29)			

2M24A.1.17 (IMGT)	GYTFTDYY (SEQ ID NO:7)	INPNSGDT (SEQ ID NO: 8)	ARNSASYSFGY (SEQ ID NO: 30)			
2M24A.1.17 (Chothia)	GYTFTDY (SEQ ID NO:13)	NPNSGD (SEQ ID NO: 14)	NSASYSFGY (SEQ ID NO: 29)			
2M24A.1.18 (Kabat)	DYYI (SEQ ID NO: 1)	WINPNSGDTNYAQKFQG (SEQ ID NO: 2)	NSGAYSFGY (SEQ ID NO: 31)			
2M24A.1.18 (IMGT)	GYTFTDYY (SEQ ID NO:7)	INPNSGDT (SEQ ID NO: 8)	ARNSGAYSFGY (SEQ ID NO: 32)			
2M24A.1.18 (Chothia)	GYTFTDY (SEQ ID NO:13)	NPNSGD (SEQ ID NO: 14)	NSGAYSFGY (SEQ ID NO: 31)			
2M24A.1.19 (Kabat)	DYYI (SEQ ID NO: 1)	WINPNSGDTNYAQKFQG (SEQ ID NO: 2)	NSGSYAFGY (SEQ ID NO: 33)			
2M24A.1.19 (IMGT)	GYTFTDYY (SEQ ID NO:7)	INPNSGDT (SEQ ID NO: 8)	ARNSGSYAFGY (SEQ ID NO: 34)			
2M24A.1.19 (Chothia)	GYTFTDY (SEQ ID NO:13)	NPNSGD (SEQ ID NO: 14)	NSGSYAFGY (SEQ ID NO: 33)			
2M24A.1.20 (Kabat)	DYYI (SEQ ID NO: 1)	WINPNSGDTNYAQKFQG (SEQ ID NO: 2)	NSGSYSAGY (SEQ ID NO: 35)			
2M24A.1.20 (IMGT)	GYTFTDYY (SEQ ID NO:7)	INPNSGDT (SEQ ID NO: 8)	ARNSGSYSAGY (SEQ ID NO: 36)			
2M24A.1.20 (Chothia)	GYTFTDY (SEQ ID NO:13)	NPNSGD (SEQ ID NO: 14)	NSGSYSAGY (SEQ ID NO: 35)			
2M24A.1.21 (Kabat)	DYYI (SEQ ID NO: 1)	WINPNSGDTNYAQKFQG (SEQ ID NO: 2)	NSGSYSFAY (SEQ ID NO: 37)			
2M24A.1.21 (IMGT)	GYTFTDYY (SEQ ID NO:7)	INPNSGDT (SEQ ID NO: 8)	ARNSGSYSFAY (SEQ ID NO: 38)			
2M24A.1.21 (Chothia)	GYTFTDY (SEQ ID NO:13)	NPNSGD (SEQ ID NO: 14)	NSGSYSFAY (SEQ ID NO: 37)			
2M24A.1.22 (Kabat)	DYYI (SEQ ID NO: 1)	WINPNSGDTNYAQKFQG	NSGSYSFGA (SEQ ID NO: 39)			

		(SEQ ID NO: 2)				
2M24A.1.22 (IMGT)	GYTFTDYY (SEQ ID NO:7)	INPNSGDT (SEQ ID NO: 8)	ARNSGSYSFGA (SEQ ID NO: 40)			
2M24A.1.22 (Chothia)	GYTFTDY (SEQ ID NO:13)	NPNSGD (SEQ ID NO: 14)	NSGSYSFGA (SEQ ID NO: 39)			
2M24A.1.5 (Kabat)				RASQGISSWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAASFPFT (SEQ ID NO: 41)
2M24A.1.5 (IMGT)				QGISSW (SEQ ID NO: 10)	GAS (SEQ ID NO: 11)	QQAASFPFT (SEQ ID NO: 41)
2M24A.1.5 (Chothia)				RASQGISSWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAASFPFT (SEQ ID NO: 41)
2M24A.1.10 (Kabat)				RASQGISSWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAFSFPFT (SEQ ID NO: 42)
2M24A.1.10 (IMGT)				QGISSW (SEQ ID NO: 10)	GAS (SEQ ID NO: 11)	QQAFSFPFT (SEQ ID NO: 42)
2M24A.1.10 (Chothia)				RASQGISSWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAFSFPFT (SEQ ID NO: 42)
2M24A.1.23 (Kabat)				RASQGISSWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	AQAYSFPFT (SEQ ID NO: 43)
2M24A.1.23 (IMGT)				QGISSW (SEQ ID NO: 10)	GAS (SEQ ID NO: 11)	AQAYSFPFT (SEQ ID NO: 43)
2M24A.1.23 (Chothia)				RASQGISSWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	AQAYSFPFT (SEQ ID NO: 43)
2M24A.1.24 (Kabat)				RASQGISSWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QAAYSFPFT (SEQ ID NO: 44)
2M24A.1.24 (IMGT)				QGISSW (SEQ ID NO: 10)	GAS (SEQ ID NO: 11)	QAAYSFPFT (SEQ ID NO: 44)
2M24A.1.24 (Chothia)				RASQGISSWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QAAYSFPFT (SEQ ID NO: 44)

2M24A.1.25 (Kabat)				RASQGISSWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYAFPFT (SEQ ID NO: 45)
2M24A.1.25 (IMGT)				QGISSW (SEQ ID NO: 10)	GAS (SEQ ID NO: 11)	QQAYAFPFT (SEQ ID NO: 45)
2M24A.1.25 (Chothia)				RASQGISSWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYAFPFT (SEQ ID NO: 45)
2M24A.1.26 (Kabat)				RASQGISSWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYSAPFT (SEQ ID NO: 46)
2M24A.1.26 (IMGT)				QGISSW (SEQ ID NO: 10)	GAS (SEQ ID NO: 11)	QQAYSAPFT (SEQ ID NO: 46)
2M24A.1.26 (Chothia)				RASQGISSWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYSAPFT (SEQ ID NO: 46)
2M24A.1.27 (Kabat)				RASQGISSWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYSFAFT (SEQ ID NO: 47)
2M24A.1.27 (IMGT)				QGISSW (SEQ ID NO: 10)	GAS (SEQ ID NO: 11)	QQAYSFAFT (SEQ ID NO: 47)
2M24A.1.27 (Chothia)				RASQGISSWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYSFAFT (SEQ ID NO: 47)
2M24A.1.28 (Kabat)				RASQGISSWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYSFPAT (SEQ ID NO: 48)
2M24A.1.28 (IMGT)				QGISSW (SEQ ID NO: 10)	GAS (SEQ ID NO: 11)	QQAYSFPAT (SEQ ID NO: 48)
2M24A.1.28 (Chothia)				RASQGISSWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYSFPAT (SEQ ID NO: 48)
2M24A.1.29 (Kabat)				RASQGISSWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYSFPFA (SEQ ID NO: 49)
2M24A.1.29 (IMGT)				QGISSW (SEQ ID NO: 10)	GAS (SEQ ID NO: 11)	QQAYSFPFA (SEQ ID NO: 49)
2M24A.1.29 (Chothia)				RASQGISSWLA	GASSLQS (SEQ ID NO: 5)	QQAYSFPFA (SEQ ID NO: 49)

				(SEQ ID NO: 4)		

Table 6. Anti-Dectin-1 antibody variable domain sequences

Name	*VH*	*VL*
2M24	QVQLVQSGAEVKKPGASVKVSCKSSGYTF TDYYIHWVRQAPGQGLEWMGWINPNSGD TNYAQKFQGRITMTRDTSISTAYLELSRLR SDDTAVFYCARNSGSYSFGYWGQGTLVT VSS (SEQ ID NO: 62)	DIQMTQSPSSVSASVGDRVTITCRAS QGISSWLAWYQQKPGKAPKLLIFGA SSLQSGVPSRFSGSGSGTDFTLTVSSL QPEDFATYYCQQAYSFPFTFGPGTKV DIE (SEQ ID NO: 64)
2M24 A.1.11	QVQLVQSGAEVKKPGASVKVSCKSSGYTF TAYYIHWVRQAPGQGLEWMGWINPNSGD TNYAQKFQGRITMTRDTSISTAYLELSRLR SDDTAVFYCARNSGSYSFGYWGQGTLVT VSS (SEQ ID NO:82)	
2M24 A.1.12	QVQLVQSGAEVKKPGASVKVSCKSSGYTF TDYYIHWVRQAPGQGLEWMGWINPNSGA TNYAQKFQGRITMTRDTSISTAYLELSRLR SDDTAVFYCARNSGSYSFGYWGQGTLVT VSS (SEQ ID NO:83)	
2M24 A.1.13	QVQLVQSGAEVKKPGASVKVSCKSSGYTF TDYYIHWVRQAPGQGLEWMGWINPNSGD TNYAQKFQGRITMTRDTSISTAYLELSRLR SDDTAVFYCARASGSYSFGYWGQGTLVT VSS (SEQ ID NO:84)	
2M24 A.1.14	QVQLVQSGAEVKKPGASVKVSCKSSGYTF TDYYIHWVRQAPGQGLEWMGWINPNSGD TNYAQKFQGRITMTRDTSISTAYLELSRLR SDDTAVFYCARNSGSASFGYWGQGTLVT VSS (SEQ ID NO:85)	
2M24 A.1.15	QVQLVQSGAEVKKPGASVKVSCKSSGYTF TDYYIHWVRQAPGQGLEWMGWINPNSGD TNYAQKFQGRITMTRDTSISTAYLELSRLR SDDTAVFYCAANSGSYSFGYWGQGTLVT VSS (SEQ ID NO:86)	
2M24 A.1.16	QVQLVQSGAEVKKPGASVKVSCKSSGYTF TDYYIHWVRQAPGQGLEWMGWINPNSGD TNYAQKFQGRITMTRDTSISTAYLELSRLR SDDTAVFYCARNAGSYSFGYWGQGTLVT VSS (SEQ ID NO:87)	
2M24 A.1.17	QVQLVQSGAEVKKPGASVKVSCKSSGYTF TDYYIHWVRQAPGQGLEWMGWINPNSGD TNYAQKFQGRITMTRDTSISTAYLELSRLR SDDTAVFYCARNSASYSFGYWGQGTLVT VSS (SEQ ID NO:88)	
2M24 A.1.18	QVQLVQSGAEVKKPGASVKVSCKSSGYTF TDYYIHWVRQAPGQGLEWMGWINPNSGD TNYAQKFQGRITMTRDTSISTAYLELSRLR SDDTAVFYCARNSGAYSFGYWGQGTLVT VSS (SEQ ID NO:89)	
2M24 A.1.19	QVQLVQSGAEVKKPGASVKVSCKSSGYTF TDYYIHWVRQAPGQGLEWMGWINPNSGD	

	TNYAQKFQGRITMTRDTSISTAYLELSRLR SDDTAVFYCARNSGSYAFGYWGQGTLVT VSS (SEQ ID NO:90)	
2M24 A.1.20	QVQLVQSGAEVKKPGASVKVSCKSSGYTF TDYYIHWVRQAPGQGLEWMGWINPNSGD TNYAQKFQGRITMTRDTSISTAYLELSRLR SDDTAVFYCARNSGSYSAGYWGQGTLVT VSS (SEQ ID NO:91)	
2M24 A.1.21	QVQLVQSGAEVKKPGASVKVSCKSSGYTF TDYYIHWVRQAPGQGLEWMGWINPNSGD TNYAQKFQGRITMTRDTSISTAYLELSRLR SDDTAVFYCARNSGSYSFAYWGQGTLVT VSS (SEQ ID NO:92)	
2M24 A.1.22	QVQLVQSGAEVKKPGASVKVSCKSSGYTF TDYYIHWVRQAPGQGLEWMGWINPNSGD TNYAQKFQGRITMTRDTSISTAYLELSRLR SDDTAVFYCARNSGSYSFGAWGQGTLVT VSS (SEQ ID NO:93)	
2M24 A.1.5		DIQMTQSPSSVSASVGDRVTITCRAS QGISSWLAWYQQKPGKAPKLLIFGA SSLQSGVPSRFSGSGSGTDFTLTVSSL QPEDFATYYCQQAASFPFTFGPGTKV DIE (SEQ ID NO:94)
2M24 A.1.10		DIQMTQSPSSVSASVGDRVTITCRAS QGISSWLAWYQQKPGKAPKLLIFGA SSLQSGVPSRFSGSGSGTDFTLTVSSL QPEDFATYYCQQAFSFPFTFGPGTKV DIE (SEQ ID NO:95)
2M24 A.1.23		DIQMTQSPSSVSASVGDRVTITCRAS QGISSWLAWYQQKPGKAPKLLIFGA SSLQSGVPSRFSGSGSGTDFTLTVSSL QPEDFATYYCAQAYSFPFTFGPGTKV DIE (SEQ ID NO:96)
2M24 A.1.24		DIQMTQSPSSVSASVGDRVTITCRAS QGISSWLAWYQQKPGKAPKLLIFGA SSLQSGVPSRFSGSGSGTDFTLTVSSL QPEDFATYYCQAAYSFPFTFGPGTKV DIE (SEQ ID NO:97)
2M24 A.1.25		DIQMTQSPSSVSASVGDRVTITCRAS QGISSWLAWYQQKPGKAPKLLIFGA SSLQSGVPSRFSGSGSGTDFTLTVSSL QPEDFATYYCQQAYAFPFTFGPGTK VDIE (SEQ ID NO:98)
2M24 A.1.26		DIQMTQSPSSVSASVGDRVTITCRAS QGISSWLAWYQQKPGKAPKLLIFGA SSLQSGVPSRFSGSGSGTDFTLTVSSL QPEDFATYYCQQAYSAPFTFGPGTK VDIE (SEQ ID NO:99)
2M24 A.1.27		DIQMTQSPSSVSASVGDRVTITCRAS QGISSWLAWYQQKPGKAPKLLIFGA SSLQSGVPSRFSGSGSGTDFTLTVSSL QPEDFATYYCQQAYSFAFTFGPGTK VDIE (SEQ ID NO:100)

2M24 A.1.28		DIQMTQSPSSVSASVGDRVTITCRAS QGISSWLAWYQQKPGKAPKLLIFGA SSLQSGVPSRFSGSGSGTDFTLTVSSL QPEDFATYYCQQAYSFPATFGPGTK VDIE (SEQ ID NO:101)
2M24 A.1.29		DIQMTQSPSSVSASVGDRVTITCRAS QGISSWLAWYQQKPGKAPKLLIFGA SSLQSGVPSRFSGSGSGTDFTLTVSSL QPEDFATYYCQQAYSFPFAFGPGTK VDIE (SEQ ID NO:102)
2M24. 1.14	QVQLVQSGAEVKKPGASVKVSCKSSGYTF TDYYIHWVRQAPGQGLEWMGWINPNSGD TNYAQKFQGRITMTRDTSISTAYLELSRLR SDDTAVFYCARNSGSASFGYWGQGTLVT VSS (SEQ ID NO:194)	DIQMTQSPSSVSASVGDRVTITCRAS QGISSWLAWYQQKPGKAPKLLIFGA SSLQSGVPSRFSGSGSGTDFTLTVSSL QPEDFATYYCQQAYSFPFTFGPGTKV DIE (SEQ ID NO: 64)
2M24. 1.15	QVQLVQSGAEVKKPGASVKVSCKSSGYTF TDYYIHWVRQAPGQGLEWMGWINPNSGD TNYAQKFQGRITMTRDTSISTAYLELSRLR SDDTAVFYCAANSGSYSFGYWGQGTLVT VSS (SEQ ID NO:195)	DIQMTQSPSSVSASVGDRVTITCRAS QGISSWLAWYQQKPGKAPKLLIFGA SSLQSGVPSRFSGSGSGTDFTLTVSSL QPEDFATYYCQQAYSFPFTFGPGTKV DIE (SEQ ID NO: 64)
2M24. 1.20	QVQLVQSGAEVKKPGASVKVSCKSSGYTF TDYYIHWVRQAPGQGLEWMGWINPNSGD TNYAQKFQGRITMTRDTSISTAYLELSRLR SDDTAVFYCARNSGSYSAGYWGQGTLVT VSS (SEQ ID NO:196)	DIQMTQSPSSVSASVGDRVTITCRAS QGISSWLAWYQQKPGKAPKLLIFGA SSLQSGVPSRFSGSGSGTDFTLTVSSL QPEDFATYYCQQAYSFPFTFGPGTKV DIE (SEQ ID NO: 64)
2M24. 1.24	QVQLVQSGAEVKKPGASVKVSCKSSGYTF TDYYIHWVRQAPGQGLEWMGWINPNSGD TNYAQKFQGRITMTRDTSISTAYLELSRLR SDDTAVFYCARNSGSYSFGYWGQGTLVT VSS (SEQ ID NO: 62)	DIQMTQSPSSVSASVGDRVTITCRAS QGISSWLAWYQQKPGKAPKLLIFGA SSLQSGVPSRFSGSGSGTDFTLTVSSL QPEDFATYYCQAAYSFPFTFGPGTKV DIE (SEQ ID NO:197)
2M24. 1.26	QVQLVQSGAEVKKPGASVKVSCKSSGYTF TDYYIHWVRQAPGQGLEWMGWINPNSGD TNYAQKFQGRITMTRDTSISTAYLELSRLR SDDTAVFYCARNSGSYSFGYWGQGTLVT VSS (SEQ ID NO: 62)	DIQMTQSPSSVSASVGDRVTITCRAS QGISSWLAWYQQKPGKAPKLLIFGA SSLQSGVPSRFSGSGSGTDFTLTVSSL QPEDFATYYCQQAYSAPFTFGPGTK VDIE (SEQ ID NO:198)

[0152] In some embodiments, an antigen binding domain, antibody, or fragment of the disclosure comprises a VH domain comprising 1, 2, or 3 CDRs from a single VH domain listed in Table 7 and/or a VL domain comprising 1, 2, or 3 CDRs from a single VL domain listed in Table 7. In some embodiments, an antigen binding domain, antibody, or fragment of the disclosure comprises a VH domain comprising 1, 2, or 3 CDRs from a single VH domain listed in Table 8 and/or a VL domain comprising 1, 2, or 3 CDRs from a single VL domain listed in Table 8. In some embodiments, an antigen binding domain, antibody, or fragment of the disclosure comprises a VH and/or VL domain listed in Table 8. As illustrated below and described herein, in some embodiments, any set of 3 VH CDRs shown in Table 7 can be combined with any set of 3 VL CDRs shown in Table 7 in an antigen binding domain, antibody, or fragment of the present disclosure. In some embodiments, any set of 3 CDRs from a VH domain shown in Table 7 can be combined with any set of 3 CDRs from a VL domain shown in Table 7 in an antigen binding domain, antibody, or fragment of the present disclosure. In some embodiments, any VH domain

shown in Table 8 can be combined with any VL domain shown in Table 8 in an antigen binding domain, antibody, or fragment of the present disclosure.

Table 7. Anti-Dectin-1 antibody CDR sequences

Name	*CDR-H1*	*CDR-H2*	*CDR-H3*	*CDR-L1*	*CDR-L2*	*CDR-L3*
2M24 (Kabat)	DYYI (SEQ ID NO: 1)	WINPNSG DTNYAQ KFQG (SEQ ID NO: 2)	NSGSYSFG Y (SEQ ID NO: 3)	RASQGIS SWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYSFPFT (SEQ ID NO: 6)
2M24 (IMGT)	GYTFTDY Y (SEQ ID NO:7)	INPNSGD T (SEQ ID NO: 8)	ARNSGSYS FGY (SEQ ID NO: 9)	QGISSW (SEQ ID NO: 10)	GAS (SEQ ID NO: 11)	QQAYSFPFT (SEQ ID NO: 12)
2M24 (Chothia)	GYTFTDY (SEQ ID NO:13)	NPNSGD (SEQ ID NO: 14)	NSGSYSFG Y (SEQ ID NO: 15)	RASQGIS SWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYSFPFT (SEQ ID NO: 6)
2M24.H1 (Kabat)	DYYI (SEQ ID NO: 1)	WINPNSG DTNYAQ KFQG (SEQ ID NO: 2)	NSGSYSFG Y (SEQ ID NO: 3)			
2M24.H1 (IMGT)	GYTFTDY Y (SEQ ID NO:7)	INPNSGD T (SEQ ID NO: 8)	ARNSGSYS FGY (SEQ ID NO: 9)			
2M24.H1 (Chothia)	GYTFTDY (SEQ ID NO:13)	NPNSGD (SEQ ID NO: 14)	NSGSYSFG Y (SEQ ID NO: 15)			
2M24.H2 (Kabat)	DYYM (SEQ ID NO: 66)	WINPNSG DTNYAQ KFQG (SEQ ID NO: 2)	NSGSYSFG Y (SEQ ID NO: 3)			
2M24.H2 (IMGT)	GYTFTDY Y (SEQ ID NO:7)	INPNSGD T (SEQ ID NO: 8)	ARNSGSYS FGY (SEQ ID NO: 9)			
2M24.H2 (Chothia)	GYTFTDY (SEQ ID NO:13)	NPNSGD (SEQ ID NO: 14)	NSGSYSFG Y (SEQ ID NO: 15)			
2M24.H3 (Kabat)	DYYI (SEQ ID NO: 1)	WINPNSG DTNYAQ KFQG (SEQ ID NO: 2)	NSGSYSFG Y (SEQ ID NO: 3)			
2M24.H3 (IMGT)	GYTFTDY Y (SEQ ID NO:7)	INPNSGD T (SEQ ID NO: 8)	ARNSGSYS FGY (SEQ ID NO: 9)			
2M24.H3 (Chothia)	GYTFTDY (SEQ ID NO:13)	NPNSGD (SEQ ID NO: 14)	NSGSYSFG Y (SEQ ID NO: 15)			

2M24.H4 (Kabat)	DYYM (SEQ ID NO: 66)	WINPNSG DTNYAQ KFQG (SEQ ID NO: 2)	NSGSYSFG Y (SEQ ID NO: 3)			
2M24.H4 (IMGT)	GYTFTDY Y (SEQ ID NO:7)	INPNSGD T (SEQ ID NO: 8)	ARNSGSYS FGY (SEQ ID NO: 9)			
2M24.H4 (Chothia)	GYTFTDY (SEQ ID NO:13)	NPNSGD (SEQ ID NO: 14)	NSGSYSFG Y (SEQ ID NO: 15)			
2M24.H5 (Kabat)	GYYM (SEQ ID NO: 67)	WINPNSG DTNYAQ KFQG (SEQ ID NO: 2)	NSGSYSFG Y (SEQ ID NO: 3)			
2M24.H5 (IMGT)	GYTFTGY Y (SEQ ID NO:68)	INPNSGD T (SEQ ID NO: 8)	ARNSGSYS FGY (SEQ ID NO: 9)			
2M24.H5 (Chothia)	GYTFTGY (SEQ ID NO:69)	NPNSGD (SEQ ID NO: 14)	NSGSYSFG Y (SEQ ID NO: 15)			
2M24.H6 (Kabat)	DYYM (SEQ ID NO: 66)	WINPNSG GTNYAQ KFQG (SEQ ID NO: 70)	NSGSYSFG Y (SEQ ID NO: 3)			
2M24.H6 (IMGT)	GYTFTDY Y (SEQ ID NO:7)	INPNSGG T (SEQ ID NO:71)	ARNSGSYS FGY (SEQ ID NO: 9)			
2M24.H6 (Chothia)	GYTFTDY (SEQ ID NO:13)	NPNSGG (SEQ ID NO: 72)	NSGSYSFG Y (SEQ ID NO: 15)			
2M24.H7 (Kabat)	GYYM (SEQ ID NO: 67)	WINPNSG GTNYAQ KFQG (SEQ ID NO: 70)	NSGSYSFG Y (SEQ ID NO: 3)			
2M24.H7 (IMGT)	GYTFTGY Y (SEQ ID NO:68)	INPNSGG T (SEQ ID NO:71)	ARNSGSYS FGY (SEQ ID NO: 9)			
2M24.H7 (Chothia)	GYTFTGY (SEQ ID NO:69)	NPNSGG (SEQ ID NO: 72)	NSGSYSFG Y (SEQ ID NO: 15)			
2M24.L1 (Kabat)				RASQGIS SWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYSFPFT (SEQ ID NO: 6)
2M24.L1 (IMGT)				QGISSW (SEQ ID NO: 10)	GAS (SEQ ID NO: 11)	QQAYSFPFT (SEQ ID NO: 12)
2M24.L1 (Chothia)				RASQGIS SWLA	GASSLQS (SEQ ID NO: 5)	QQAYSFPFT (SEQ ID NO: 6)

				(SEQ ID NO: 4)		
2M24.L2 (Kabat)				RASQGISSWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYSFPFT (SEQ ID NO: 6)
2M24.L2 (IMGT)				QGISSW (SEQ ID NO: 10)	GAS (SEQ ID NO: 11)	QQAYSFPFT (SEQ ID NO: 12)
2M24.L2 (Chothia)				RASQGISSWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYSFPFT (SEQ ID NO: 6)
2M24.L3 (Kabat)				RASQGISSWLA (SEQ ID NO: 4)	AASSLQS (SEQ ID NO: 73)	QQAYSFPFT (SEQ ID NO: 6)
2M24.L3 (IMGT)				QGISSW (SEQ ID NO: 10)	AAS (SEQ ID NO: 74)	QQAYSFPFT (SEQ ID NO: 12)
2M24.L3 (Chothia)				RASQGISSWLA (SEQ ID NO: 4)	AASSLQS (SEQ ID NO: 75)	QQAYSFPFT (SEQ ID NO: 6)
2M24.L4 (Kabat)				RASQGISSWLA (SEQ ID NO: 4)	AASSLQS (SEQ ID NO: 73)	QQAYSFPFT (SEQ ID NO: 6)
2M24.L4 (IMGT)				QGISSW (SEQ ID NO: 10)	AAS (SEQ ID NO: 74)	QQAYSFPFT (SEQ ID NO: 12)
2M24.L4 (Chothia)				RASQGISSWLA (SEQ ID NO: 4)	AASSLQS (SEQ ID NO: 75)	QQAYSFPFT (SEQ ID NO: 6)

Table 8. Anti-Dectin-1 antibody variable domain sequences

Name	*VH*	*VL*
2M24	QVQLVQSGAEVKKPGASVKVSCKSSGYTFTDYYIHWVRQAPGQGLEWMGWINPNSGDTNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGQGTLVTVSS (SEQ ID NO: 62)	DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPSRFSGSGSGTDFTLTVSSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO: 64)
2M24.H1	QVQLVQSGAEVKKPGASVKVSCKSSGYTFTDYYIHWVRQAPGQGLEWMGWINPNSGDTNYAQKFQGRVTMTRDTSISTAYMELSRLRSDDTAVYYCARNSGSYSFGYWGQGTLVTVSS (SEQ ID NO:103)	
2M24.H2	QVQLVQSGAEVKKPGASVKVSCKASGYTFTDYYMHWVRQAPGQGLEWMGWINPNSGDTNYAQKFQGRVTMTRDTSISTAYMELS	

	RLRSDDTAVYYCARNSGSYSFGYWGQGT LVTVSS (SEQ ID NO:104)	
2M24. H3	QVQLVQSGAEVKKPGASVKVSCKASGYT FTDYYIHWVRQAPGQGLEWMGWINPNSG DTNYAQKFQGRVTMTRDTSISTAYMELSR LRSDDTAVYYCARNSGSYSFGYWGQGTL VTVSS (SEQ ID NO:105)	
2M24. H4	QVQLVQSGAEVKKPGASVKVSCKSSGYTF TDYYMHWVRQAPGQGLEWMGWINPNSG DTNYAQKFQGRVTMTRDTSISTAYMELSR LRSDDTAVYYCARNSGSYSFGYWGQGTL VTVSS (SEQ ID NO:106)	
2M24. H5	QVQLVQSGAEVKKPGASVKVSCKASGYT FTGYYMHWVRQAPGQGLEWMGWINPNS GDTNYAQKFQGRVTMTRDTSISTAYMELS RLRSDDTAVYYCARNSGSYSFGYWGQGT LVTVSS (SEQ ID NO:107)	
2M24. H6	QVQLVQSGAEVKKPGASVKVSCKASGYT FTDYYMHWVRQAPGQGLEWMGWINPNS GGTNYAQKFQGRVTMTRDTSISTAYMELS RLRSDDTAVYYCARNSGSYSFGYWGQGT LVTVSS (SEQ ID NO:108)	
2M24. H7	QVQLVQSGAEVKKPGASVKVSCKASGYT FTGYYMHWVRQAPGQGLEWMGWINPNS GGTNYAQKFQGRVTMTRDTSISTAYMELS RLRSDDTAVYYCARNSGSYSFGYWGQGT LVTVSS (SEQ ID NO:109)	
2M24. L1		DIQMTQSPSSVSASVGDRVTITCRAS QGISSWLAWYQQKPGKAPKLLIFGA SSLQSGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQAYSFPFTFGPGTKV DIE (SEQ ID NO:110)
2M24. L2		DIQMTQSPSSVSASVGDRVTITCRAS QGISSWLAWYQQKPGKAPKLLIYGA SSLQSGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQAYSFPFTFGPGTKV DIE (SEQ ID NO:111)
2M24. L3		DIQMTQSPSSVSASVGDRVTITCRAS QGISSWLAWYQQKPGKAPKLLIFAA SSLQSGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQAYSFPFTFGPGTKV DIE (SEQ ID NO:112)
2M24. L4		DIQMTQSPSSVSASVGDRVTITCRAS QGISSWLAWYQQKPGKAPKLLIYAA SSLQSGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQAYSFPFTFGPGTKV DIE (SEQ ID NO:113)

[0153] In some embodiments, the antigen binding domain, antibody, or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises: a CDR-H1 comprising the amino acid sequence of DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence of WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the

amino acid sequence of NSGSASFGY (SEQ ID NO: 187); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence of QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the antigen binding domain, antibody, or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises: a CDR-H1 comprising the amino acid sequence of DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence of WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence of NSGSYSAGY (SEQ ID NO: 190); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence of QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the antigen binding domain, antibody, or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises: a CDR-H1 comprising the amino acid sequence of DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence of WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence of NSGSYSFGY (SEQ ID NO: 3); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence of QAAYSFPFT (SEQ ID NO: 192). In some embodiments, the antigen binding domain, antibody, or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises: a CDR-H1 comprising the amino acid sequence of DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence of WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence of NSGSYSFGY (SEQ ID NO: 3); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence of QQAYSAPFT (SEQ ID NO: 193). In some embodiments, the antigen binding domain, antibody, or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises: a CDR-H1 comprising the amino acid sequence of DYYM (SEQ ID NO: 199), a CDR-H2 comprising the amino acid sequence of WINPNEGDTNYAQKFEG (SEQ ID NO: 200), and a CDR-H3 comprising the amino acid sequence of NTGAYSFGY (SEQ ID NO: 204); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASDLQS (SEQ ID NO: 206), and a CDR-L3 comprising the amino acid sequence of QQAYGFPFT (SEQ ID NO: 207). In some embodiments, the antigen binding domain, antibody, or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises: a CDR-H1 comprising the amino acid sequence of DYYM (SEQ ID NO: 199), a CDR-H2 comprising the amino acid sequence of WINPNEGDTNYAQKFQE (SEQ ID NO: 201), and a

CDR-H3 comprising the amino acid sequence of NTGAYSFGY (SEQ ID NO: 204); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASDLQS (SEQ ID NO: 206), and a CDR-L3 comprising the amino acid sequence of HQAYSFPFT (SEQ ID NO: 208).

[0154] In some embodiments, the antigen binding domain, antibody, or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises: a CDR-H1 comprising the amino acid sequence of GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence of INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence of ARNSGSASFGY (SEQ ID NO: 188); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence of QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence of GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence of QQAYSFPFT (SEQ ID NO: 12). In some embodiments, the antigen binding domain, antibody, or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises: a CDR-H1 comprising the amino acid sequence of GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence of INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence of AANSGSYSFGY (SEQ ID NO: 189); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence of QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence of GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence of QQAYSFPFT (SEQ ID NO: 12). In some embodiments, the antigen binding domain, antibody, or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises: a CDR-H1 comprising the amino acid sequence of GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence of INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence of ARNSGSYSAGY (SEQ ID NO: 191); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence of QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence of GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence of QQAYSFPFT (SEQ ID NO: 12). In some embodiments, the antigen binding domain, antibody, or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises: a CDR-H1 comprising the amino acid sequence of GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence of INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence of ARNSGSYSFGY (SEQ ID NO: 9); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence of QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence of GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence of QAAYSFPFT (SEQ ID NO: 192). In some embodiments, the antigen binding domain, antibody, or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises: a CDR-H1 comprising the amino acid sequence of GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence of INPNSGDT (SEQ ID NO: 8), and a CDR-H3 comprising the amino acid sequence of ARNSGSYSFGY

(SEQ ID NO: 9); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence of QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence of GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence of QQAYSAPFT (SEQ ID NO: 193). In some embodiments, the antigen binding domain, antibody, or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises: a CDR-H1 comprising the amino acid sequence of GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence of INPNEGDT (SEQ ID NO: 202), and a CDR-H3 comprising the amino acid sequence of ARNTGAYSFGY (SEQ ID NO: 205); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence of QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence of GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence of QQAYGFPFT (SEQ ID NO: 207). In some embodiments, the antigen binding domain, antibody, or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises: a CDR-H1 comprising the amino acid sequence of GYTFTDYY (SEQ ID NO:7), a CDR-H2 comprising the amino acid sequence of INPNEGDT (SEQ ID NO: 202), and a CDR-H3 comprising the amino acid sequence of ARNTGAYSFGY (SEQ ID NO: 205); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence of QGISSW (SEQ ID NO: 10), a CDR-L2 comprising the amino acid sequence of GAS (SEQ ID NO: 11), and a CDR-L3 comprising the amino acid sequence of HQAYSFPFT (SEQ ID NO: 208).

[0155] In some embodiments, the antigen binding domain, antibody, or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises: a CDR-H1 comprising the amino acid sequence of GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence of NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence of NSGSASFGY (SEQ ID NO: 187); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence of QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the antigen binding domain, antibody, or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises: a CDR-H1 comprising the amino acid sequence of GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence of NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence of NSGSYSAGY (SEQ ID NO: 190); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence of QQAYSFPFT (SEQ ID NO: 6). In some embodiments, the antigen binding domain, antibody, or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises: a CDR-H1 comprising the amino acid sequence of GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence of NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence of NSGSYSFGY (SEQ ID NO: 15); and wherein

the VL domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence of QAAYSFPFT (SEQ ID NO: 192). In some embodiments, the antigen binding domain, antibody, or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises: a CDR-H1 comprising the amino acid sequence of GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence of NPNSGD (SEQ ID NO: 14), and a CDR-H3 comprising the amino acid sequence of NSGSYSFGY (SEQ ID NO: 15); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence of QQAYSAPFT (SEQ ID NO: 193). In some embodiments, the antigen binding domain, antibody, or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises: a CDR-H1 comprising the amino acid sequence of GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence of NPNEGD (SEQ ID NO: 203), and a CDR-H3 comprising the amino acid sequence of NTGAYSFGY (SEQ ID NO: 204); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASDLQS (SEQ ID NO: 206), and a CDR-L3 comprising the amino acid sequence of QQAYGFPFT (SEQ ID NO: 207). In some embodiments, the antigen binding domain, antibody, or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises: a CDR-H1 comprising the amino acid sequence of GYTFTDY (SEQ ID NO:13), a CDR-H2 comprising the amino acid sequence of NPNEGD (SEQ ID NO: 203), and a CDR-H3 comprising the amino acid sequence of NTGAYSFGY (SEQ ID NO: 204); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASDLQS (SEQ ID NO: 206), and a CDR-L3 comprising the amino acid sequence of HQAYSFPFT (SEQ ID NO: 208).

[0156] In some embodiments, the VH domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos: 62, 103-109, 194-196, 209, 211, 213, 215, and 220. In some embodiments, the VL domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos:64, 110-113, 197, 198, 210, 212, 214, 216, and 221. In some embodiments, the VH domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos: 62, 103-109, 194-196, 209, 211, 213, 215, and 220, and the VL domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos:64, 110-113, 197, 198, 210, 212, 214, 216, and 221. In some embodiments, the VH domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos: 62, 194-196, 209, 211, 213, 215, and 220. In some embodiments, the VL domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos:64, 197, 198, 210, 212, 214, 216, and 221. In some embodiments, the VH domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos: 62, 194-196, 209, 211, 213, 215, and 220, and the VL domain comprises

an amino acid sequence selected from the group consisting of SEQ ID Nos:64, 197, 198, 210, 212, 214, 216, and 221. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 194, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 195, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 196, and the VL domain comprises the amino acid sequence of SEQ ID NO:64. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 62, and the VL domain comprises the amino acid sequence of SEQ ID NO:197. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 62, and the VL domain comprises the amino acid sequence of SEQ ID NO:198. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 209, and the VL domain comprises the amino acid sequence of SEQ ID NO:210. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 211, and the VL domain comprises the amino acid sequence of SEQ ID NO:212. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 213, and the VL domain comprises the amino acid sequence of SEQ ID NO:214. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 213, and the VL domain comprises the amino acid sequence of SEQ ID NO:214. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 215, and the VL domain comprises the amino acid sequence of SEQ ID NO:216. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 220, and the VL domain comprises the amino acid sequence of SEQ ID NO:221.

[0157] In some embodiments, an antigen binding domain, antibody, or fragment of the disclosure comprises a VH domain comprising 1, 2, or 3 CDRs from a single VH domain listed in Table A and/or a VL domain comprising 1, 2, or 3 CDRs from a single VL domain listed in Table A. In some embodiments, an antigen binding domain, antibody, or fragment of the disclosure comprises a VH domain comprising 1, 2, or 3 CDRs from a single VH domain listed in Table B and/or a VL domain comprising 1, 2, or 3 CDRs from a single VL domain listed in Table B. In some embodiments, an antigen binding domain, antibody, or fragment of the disclosure comprises a VH and/or VL domain listed in Table B. As illustrated below and described herein, in some embodiments, any set of 3 VH CDRs shown in Table A can be combined with any set of 3 VL CDRs shown in Table A in an antigen binding domain, antibody, or fragment of the present disclosure. In some embodiments, any set of 3 CDRs from a VH domain shown in Table A can be combined with any set of 3 CDRs from a VL domain shown in Table A in an antigen binding domain, antibody, or fragment of the present disclosure. In some embodiments, any VH domain shown in Table B can be combined with any VL domain shown in Table B in an antigen binding domain, antibody, or fragment of the present disclosure.

Table A. Anti-Dectin-1 2M24 variant antibody CDR sequences

Name	*CDR-H1*	*CDR-H2*	*CDR-H3*	*CDR-L1*	*CDR-L2*	*CDR-L3*
2M24 (Kabat)	DYYI (SEQ ID NO: 1)	WINPNSG DTNYAQ KFQG (SEQ ID NO: 2)	NSGSYSFG Y (SEQ ID NO: 3)	RASQGIS SWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYSFPFT (SEQ ID NO: 6)
2M24 (IMGT)	GYTFTDY Y (SEQ ID NO:7)	INPNSGD T (SEQ ID NO: 8)	ARNSGSYS FGY (SEQ ID NO: 9)	QGISSW (SEQ ID NO: 10)	GAS (SEQ ID NO: 11)	QQAYSFPFT (SEQ ID NO: 12)
2M24 (Chothia)	GYTFTDY (SEQ ID NO:13)	NPNSGD (SEQ ID NO: 14)	NSGSYSFG Y (SEQ ID NO: 15)	RASQGIS SWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYSFPFT (SEQ ID NO: 6)
2M24.1.14 (Kabat)	DYYI (SEQ ID NO: 1)	WINPNSG DTNYAQ KFQG (SEQ ID NO: 2)	NSGSASFG Y (SEQ ID NO: 187)	RASQGIS SWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYSFPFT (SEQ ID NO: 6)
2M24.1.14 (IMGT)	GYTFTDY Y (SEQ ID NO:7)	INPNSGD T (SEQ ID NO: 8)	ARNSGSAS FGY (SEQ ID NO: 188)	QGISSW (SEQ ID NO: 10)	GAS (SEQ ID NO: 11)	QQAYSFPFT (SEQ ID NO: 12)
2M24.1.14 (Chothia)	GYTFTDY (SEQ ID NO:13)	NPNSGD (SEQ ID NO: 14)	NSGSASFG Y (SEQ ID NO: 187)	RASQGIS SWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYSFPFT (SEQ ID NO: 6)
2M24.1.15 (Kabat)	DYYI (SEQ ID NO: 1)	WINPNSG DTNYAQ KFQG (SEQ ID NO: 2)	NSGSYSFG Y (SEQ ID NO: 3)	RASQGIS SWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYSFPFT (SEQ ID NO: 6)
2M24.1.15 (IMGT)	GYTFTDY Y (SEQ ID NO:7)	INPNSGD T (SEQ ID NO: 8)	AANSGSYS FGY (SEQ ID NO: 189)	QGISSW (SEQ ID NO: 10)	GAS (SEQ ID NO: 11)	QQAYSFPFT (SEQ ID NO: 12)
2M24.1.15 (Chothia)	GYTFTDY (SEQ ID NO:13)	NPNSGD (SEQ ID NO: 14)	NSGSYSFG Y (SEQ ID NO: 15)	RASQGIS SWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYSFPFT (SEQ ID NO: 6)
2M24.1.20 (Kabat)	DYYI (SEQ ID NO: 1)	WINPNSG DTNYAQ KFQG (SEQ ID NO: 2)	NSGSYSAG Y (SEQ ID NO: 190)	RASQGIS SWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYSFPFT (SEQ ID NO: 6)
2M24.1.20 (IMGT)	GYTFTDY Y (SEQ ID NO:7)	INPNSGD T (SEQ ID NO: 8)	ARNSGSYS AGY (SEQ ID NO: 191)	QGISSW (SEQ ID NO: 10)	GAS (SEQ ID NO: 11)	QQAYSFPFT (SEQ ID NO: 12)
2M24.1.20 (Chothia)	GYTFTDY (SEQ ID NO:13)	NPNSGD (SEQ ID NO: 14)	NSGSYSAG Y (SEQ ID NO: 190)	RASQGIS SWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYSFPFT (SEQ ID NO: 6)
2M24.1.24 (Kabat)	DYYI (SEQ ID NO: 1)	WINPNSG DTNYAQ KFQG (SEQ ID NO: 2)	NSGSYSFG Y (SEQ ID NO: 3)	RASQGIS SWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QAAYSFPFT (SEQ ID NO: 192)

2M24.1.24 (IMGT)	GYTFTDYY (SEQ ID NO:7)	INPNSGDT (SEQ ID NO: 8)	ARNSGSYSFGY (SEQ ID NO: 9)	QGISSW (SEQ ID NO: 10)	GAS (SEQ ID NO: 11)	QAAYSFPFT (SEQ ID NO: 192)
2M24.1.24 (Chothia)	GYTFTDY (SEQ ID NO:13)	NPNSGD (SEQ ID NO: 14)	NSGSYSFGY (SEQ ID NO: 15)	RASQGISSWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QAAYSFPFT (SEQ ID NO: 192)
2M24.1.26 (Kabat)	DYYI (SEQ ID NO: 1)	WINPNSGDTNYAQKFQG (SEQ ID NO: 2)	NSGSYSFGY (SEQ ID NO: 3)	RASQGISSWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYSAPFT (SEQ ID NO: 193)
2M24.1.26 (IMGT)	GYTFTDYY (SEQ ID NO:7)	INPNSGDT (SEQ ID NO: 8)	ARNSGSYSFGY (SEQ ID NO: 9)	QGISSW (SEQ ID NO: 10)	GAS (SEQ ID NO: 11)	QQAYSAPFT (SEQ ID NO: 193)
2M24.1.26 (Chothia)	GYTFTDY (SEQ ID NO:13)	NPNSGD (SEQ ID NO: 14)	NSGSYSFGY (SEQ ID NO: 15)	RASQGISSWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYSAPFT (SEQ ID NO: 193)
2M24.119 (Kabat)	DYYM (SEQ ID NO: 199)	WINPNEGDTNYAQKFEG (SEQ ID NO: 200)	NTGAYSFGY (SEQ ID NO: 204)	RASQGISSWLA (SEQ ID NO: 4)	GASDLQS (SEQ ID NO: 206)	QQAYGFPFT (SEQ ID NO: 207)
2M24.119 (IMGT)	GYTFTDYY (SEQ ID NO:7)	INPNEGDT (SEQ ID NO: 202)	ARNTGAYSFGY (SEQ ID NO: 205)	QGISSW (SEQ ID NO: 10)	GAS (SEQ ID NO: 11)	QQAYGFPFT (SEQ ID NO: 207)
2M24.119 (Chothia)	GYTFTDY (SEQ ID NO:13)	NPNEGD (SEQ ID NO: 203)	NTGAYSFGY (SEQ ID NO: 204)	RASQGISSWLA (SEQ ID NO: 4)	GASDLQS (SEQ ID NO: 206)	QQAYGFPFT (SEQ ID NO: 207)
2M24.116 (Kabat)	DYYM (SEQ ID NO: 199)	WINPNEGDTNYAQKFQE (SEQ ID NO: 201)	NTGAYSFGY (SEQ ID NO: 204)	RASQGISSWLA (SEQ ID NO: 4)	GASDLQS (SEQ ID NO: 206)	HQAYSFPFT (SEQ ID NO: 208)
2M24.116 (IMGT)	GYTFTDYY (SEQ ID NO:7)	INPNEGDT (SEQ ID NO: 202)	ARNTGAYSFGY (SEQ ID NO: 205)	QGISSW (SEQ ID NO: 10)	GAS (SEQ ID NO: 11)	HQAYSFPFT (SEQ ID NO: 208)
2M24.116 (Chothia)	GYTFTDY (SEQ ID NO:13)	NPNEGD (SEQ ID NO: 203)	NTGAYSFGY (SEQ ID NO: 204)	RASQGISSWLA (SEQ ID NO: 4)	GASDLQS (SEQ ID NO: 206)	HQAYSFPFT (SEQ ID NO: 208)

Table B. Anti-Dectin-1 2M24 variant antibody variable domain sequences

Name	*VH*	*VL*
2M24	QVQLVQSGAEVKKPGASVKVSCKSSGYTFTDYYIHWVRQAPGQGLEWMGWINPNSGDTNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGQGTLVTVSS (SEQ ID NO: 62)	DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPSRFSGSGSGTDFTLTVSSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO: 64)

2M24.1.14	QVQLVQSGAEVKKPGASVKVSCKSSGYTFTDYYIHWVRQAPGQGLEWMGWINPNSGDTNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSASFGYWGQGTLVTVSS (SEQ ID NO:194)	DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPSRFSGSGSGTDFTLTVSSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO: 64)
2M24.1.15	QVQLVQSGAEVKKPGASVKVSCKSSGYTFTDYYIHWVRQAPGQGLEWMGWINPNSGDTNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCAANSGSYSFGYWGQGTLVTVSS (SEQ ID NO:195)	DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPSRFSGSGSGTDFTLTVSSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO: 64)
2M24.1.20	QVQLVQSGAEVKKPGASVKVSCKSSGYTFTDYYIHWVRQAPGQGLEWMGWINPNSGDTNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSAGYWGQGTLVTVSS (SEQ ID NO:196)	DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPSRFSGSGSGTDFTLTVSSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO: 64)
2M24.1.24	QVQLVQSGAEVKKPGASVKVSCKSSGYTFTDYYIHWVRQAPGQGLEWMGWINPNSGDTNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGQGTLVTVSS (SEQ ID NO: 62)	DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPSRFSGSGSGTDFTLTVSSLQPEDFATYYCQAAYSFPFTFGPGTKVDIE (SEQ ID NO:197)
2M24.1.26	QVQLVQSGAEVKKPGASVKVSCKSSGYTFTDYYIHWVRQAPGQGLEWMGWINPNSGDTNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGQGTLVTVSS (SEQ ID NO: 62)	DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPSRFSGSGSGTDFTLTVSSLQPEDFATYYCQQAYSAPFTFGPGTKVDIE (SEQ ID NO:198)
2M24.119	QVQLVQSGAEVKKPGASVKVSCKASGYTFTDYYMHWVRQAPGQGLEWMGWINPNEGDTNYAQKFEGRITMTRDTSISTAYMELSRLRSDDTAVYYCARNTGAYSFGYWGQGTLVTVSS (SEQ ID NO:209)	DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIYGASDLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQAYGFPFTFGPGTKVDIK (SEQ ID NO:210)
2M24.116	QVQLVQSGAEVKKPGASVKVSCKASGYTFTDYYMHWVRQAPGQGLEWMGWINPNEGDTNYAQKFQERITMTRDTSISTAYMELSRLRSDDTAVYYCARNTGAYSFGYWGQGTLVTVSS (SEQ ID NO:211)	DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIYGASDLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCHQAYSFPFTFGPGTKVDIK (SEQ ID NO:212)
2M24 P1	QVQLVQSGAEVKKPGASVKVSCKSSGYTFTDYYIHWVRQAPGQGLEWMGWINPNSGDTNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGCGTLVTVSS (SEQ ID NO:213)	DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKCPKLLIFGASSLQSGVPSRFSGSGSGTDFTLTVSSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO:214)
2M24 P2	QVQLVQSGAEVKKPGASVKVSCKSSGYTFTDYYIHWVRQAPGQGCEWMGWINPNSGDTNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGQGTLVTVSS (SEQ ID NO:215)	DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPSRFSGSGSGTDFTLTVSSLQPEDFATYYCQQAYSFPFTCGPGTKVDIE (SEQ ID NO:216)
2M24.119 with P1	QVQLVQSGAEVKKPGASVKVSCKASGYTFTDYYMHWVRQAPGQGLEWMGWINPNEGDTNYAQKFEGRITMTRDTSISTAYMELSRLRSDDTAVYYCARNTGAYSFGYWGCGTLVTVSS (SEQ ID NO:220)	DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKCPKLLIYGASDLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQAYGFPFTFGPGTKVDIK (SEQ ID NO:221)

[0158] In some embodiments, the multispecific binding protein, antigen binding domain, antibody, or antibody fragment binds to human Dectin-1. In some embodiments, the multispecific binding protein,

antigen binding domain, antibody, or antibody fragment binds to human Dectin-1 expressed on the surface of a macrophage, monocyte, dendritic cell, or granulocyte. In some embodiments, the multispecific binding protein, antigen binding domain, antibody, or antibody fragment binds to human Dectin-1 isoform A and/or human Dectin-1 isoform B. In some embodiments, human Dectin-1 isoform A comprises the amino acid sequence MEYHPDLENLDEDGYTQLHFDSQSNTRIAVVSEKGSCAASPPWRLIAVILGILCLVILVIAVVLGT MAIWRSNSGSNTLENGYFLSRNKENHSQPTQSSLEDSVTPTKAVKTTGVLSSPCPPNWIIYEKSCY LFSMSLNSWDGSKRQCWQLGSNLLKIDSSNELGFIVKQVSSQPDNSFWIGLSRPQTEVPWLWED GSTFSSNLFQIRTTATQENPSPNCVWIHVSVIYDQLCSVPSYSICEKKFSM (SEQ ID NO:185). In some embodiments, human Dectin-1 isoform B comprises the amino acid sequence MEYHPDLENLDEDGYTQLHFDSQSNTRIAVVSEKGSCAASPPWRLIAVILGILCLVILVIAVVLGT MGVLSSPCPPNWIIYEKSCYLFSMSLNSWDGSKRQCWQLGSNLLKIDSSNELGFIVKQVSSQPDN SFWIGLSRPQTEVPWLWEDGSTFSSNLFQIRTTATQENPSPNCVWIHVSVIYDQLCSVPSYSICEKK FSM (SEQ ID NO:186).

[0159] In some embodiments, the antigen binding domain, antibody, or antibody fragment binds to human Dectin-1 expressed on the surface of a cell with an EC50 of less than 5nM, less than 2nM, less than 1nM, or less than 0.5nM. In some embodiments, the antigen binding domain, antibody, or antibody fragment is capable of binding to human Dectin-1 and monkey Dectin-1, *e.g.*, cynomolgus Dectin-1.

[0160] Examples of antibody fragments include, but are not limited to, Fab, Fab', F(ab')2, and Fv fragments, Fab'-SH, F(ab')2, diabodies, linear antibodies, single chain antibodies, nanobodies, scFv fragments, VH, and multispecific (*e.g.*, bispecific) antibodies/fragments formed from antibody fragments.

[0161] A "Fab" (fragment antigen binding) is a portion of an antibody that binds to antigens and includes the variable region and CH1 of the heavy chain linked to the light chain via an inter-chain disulfide bond.

[0162] In some embodiments, an antibody of the present disclosure comprises an Fc region. An antibody may be of any class or subclass, including IgG and subclasses thereof (IgG1, IgG2, IgG3, IgG4), IgM, IgE, IgA, and IgD. An immunoglobulin Fc region of the molecule that causes targeted phagocytosis may have important role in the process by engaging Fc receptors and inducing additional phagocytosis. In some embodiments, the molecule has a modified Fc region that has reduced ADCC activity as compared to a wild type human IgG1 (*e.g.*, comprising one or more mutations reducing effector function as described herein).

[0163] In some embodiments, an antibody of the present disclosure comprises an Fc region wherein a carbohydrate structure attached to the Fc region has reduced fucose or lacks fucose, *e.g.*, at least one or two of the heavy chains of the antibody is non-fucosylated or comprise reduced fucosylation. In some embodiments, provided herein is a composition comprising an antibody of the present disclosure that comprises an Fc region wherein a carbohydrate structure attached to the Fc region has reduced fucose or lacks fucose, *e.g.*, at least one or two of the heavy chains of the antibody is/are non-fucosylated or

comprise(s) reduced fucosylation. In some embodiments, less than 50% of the N-glycoside-linked carbohydrate chains in the composition contain a fucose residue. In some embodiments, substantially none of the N-glycoside-linked carbohydrate chains contain a fucose residue. In some embodiments, an antibody with reduced fucose or lacking fucose has improved ADCC function.

[0164] In some embodiments, the antibody further comprises an Fc region. In some embodiments, the Fc region is a human IgG Fc region. In some embodiments, the Fc region is a human IgG1 or human IgG4 Fc region. In some embodiments, the Fc region is a human IgG1 Fc region comprising S239D and I332E substitutions, according to EU numbering. In some embodiments, the Fc region is a human IgG1 Fc region comprising S239D, A330L, and I332E substitutions, according to EU numbering. In some embodiments, the Fc region is a human IgG1 Fc region comprising G236A, S239D, A330L, and I332E substitutions, according to EU numbering. In some embodiments, the Fc region is a human IgG4 Fc region comprising an S228P substitution, according to EU numbering.

[0165] In other embodiments, an antibody of the present disclosure (*e.g.*, an IgG1 antibody) or composition comprising an antibody of the present disclosure (*e.g.*, an IgG1 antibody) comprises wild-type glycosylation of the Fc region. In some embodiments, provided herein are fucosylated antibodies of the present disclosure (*e.g.*, an IgG1 antibody) or compositions comprising a fucosylated antibody of the present disclosure (*e.g.*, an IgG1 antibody).

[0166] Fucosylation or fucosylated antibodies can refer to the presence of fucose residues within the oligosaccharides attached to the peptide backbone of an antibody. Specifically, a fucosylated antibody comprises α (1,6)-linked fucose at the innermost N-acetylglucosamine (GlcNAc) residue in one or both of the N-linked oligosaccharides attached to the antibody Fc region, e.g., at position Asn 297 of the human IgG1 Fc region (EU numbering of Fc region residues). Asn297 may also be located about + 3 amino acids upstream or downstream of position 297, i.e., between positions 294 and 300, due to minor sequence variations in immunoglobulins. Non-fucosylated or fucose-deficient antibodies have reduced fucose relative to the amount of fucose on the same antibody produced in a cell line. Antibody fucosylation can be measured, *e.g.*, in an N-glycosidase F treated antibody composition assessed by matrix-assisted laser desorption-ionization time-of-flight mass spectrometry (MALDI TOF MS).

[0167] In some embodiments, the Fc region comprises one or more mutations that reduce or eliminate fucosylation, *e.g.*, a substitution at Asn 297 of the human IgG1 Fc region (EU numbering of Fc region residues). Optionally, the Fc region further comprises one or more amino acid substitutions therein which further improve ADCC, for example, substitutions at positions 298, 333, and/or 334 of the Fc region (Eu numbering of residues). Examples of publications related to "defucosylated" or "fucose-deficient" antibodies include: US 2003/0157108; WO 2000/61739; WO 2001/29246; US 2003/0115614; US 2002/0164328; US 2004/0093621; US 2004/0132140; US 2004/0110704; US 2004/0110282; US 2004/0109865; WO 2003/085119; WO 2003/084570; WO 2005/035586; WO 2005/035778; WO2005/053742; Okazaki et al. J. Mol. Biol. 336:1239-1249 (2004); Yamane-Ohnuki et al. Biotech. Bioeng. 87: 614 (2004).

[0168] In some embodiments, the afucosylated or non-fucosylated antibody is produced in a cell line with a genetic modification that results in an afucosylated or non-fucosylated antibody. Examples of cell lines producing afucosylated antibodies include Lec13 CHO cells deficient in protein fucosylation (Ripka et al. Arch. Biochem. Biophys. 249:533-545 (1986); US Pat Appl No US 2003/0157108 A1, Presta, L; and WO 2004/056312 A1, Adams et al., especially at Example 11), and knockout cell lines, such as alpha-1,6-fucosyltransferase gene, FUT8, knockout CHO cells (Yamane-Ohnuki et al. Biotech. Bioeng. 87: 614 (2004)), cells overexpressing β1,4-N-acetylglucosaminyltransferase III (GnT-III) and Golgi μ-mannosidase II (ManII), and cells with a knockout in the mannosyl-glycoprotein 2-beta-N-acetylglucosaminyltranferase (MGAT1; *see* Byrne, G. *et al.* (2018) *PLoS Biol.* 16:e2005817).

[0169] In some embodiments, the afucosylated or non-fucosylated antibody is produced in a cell line treated with an inhibitor of glycoprocessing enzyme(s), such as kifunensine, which is an inhibitor of mannosidase I (*see, e.g.,* Elbein, A.D. *et al.* (1990) *J. Biol. Chem.* 265:15599-15605). For example, cells can be centrifuged and resuspended in growth medium comprising kifunensine (*e.g.*, at 250μg/mL), then cultured and used for antibody production.

[0170] In certain aspects, the present disclosure provides multispecific (*e.g.*, bispecific) antibodies and antibody fragments comprising a first antigen-binding domain that binds to a first target of interest and a second antigen-binding domain that binds to a second target of interest. In some embodiments, the present disclosure provides multispecific (*e.g.*, bispecific) antibodies and antibody fragments comprising a first antigen-binding domain that binds to human Dectin-1 and a second antigen-binding domain that binds to a target of interest.

[0171] In some embodiments, multispecific (*e.g.*, bispecific) antibodies and antibody fragments comprise a first antibody or antigen-binding fragment comprising the first antigen-binding domain and a second antibody or antigen-binding fragment comprising the second antigen-binding domain. In some embodiments, the first antibody or fragment is coupled to avidin, streptavidin, neutravidin, or a biotin-binding derivative thereof, and the second antibody or fragment is coupled to biotin or an avidin-binding derivative thereof. In some embodiments, the second antibody or fragment is coupled to avidin, streptavidin, neutravidin, or a biotin-binding derivative thereof, and the first antibody or fragment is coupled to biotin or an avidin-binding derivative thereof. In some embodiments, the first antibody or fragment is bound to the second antibody or fragment via an interaction between the avidin, streptavidin, neutravidin, or biotin-binding derivative thereof and the biotin or avidin-binding derivative thereof.

[0172] Exemplary avidins, streptavidins, neutravidins, or biotin-binding derivatives thereof are known in the art. In some embodiments, the streptavidin is monomeric streptavidin (mSA). Exemplary biotins or avidin-binding derivatives thereof are known in the art. In some embodiments, an antibody or antigen-binding fragment thereof of the present disclosure is biotinylated. Kits for biotinylating an antibody of interest are known in the art and commercially available. In some embodiments, mSA comprises the sequence

EFASAEAGITGTWYNQHGSTFTVTAGADGNLTGQYENRAQGTGCQNSPYTLTGRYNGTKLEWR

VEWNNSTENCHSRTEWRGQYQGGAEARINTQWNLTYEGGSGPATEQGQDTFTKVKPSAASGS (SEQ ID NO:120).

[0173] In some embodiments, one or both of the first and second antigen binding domain, antibody, or fragment is/are humanized.

[0174] In some embodiments, one or both of the first and second antigen binding domain, antibody, or fragment comprise(s) a tag, *e.g.*, for affinity purification. In some embodiments, the tag is a polyhistidine tag.

[0175] In some embodiments, one or both of the first and second antibodies or fragments are Fab, Fab', F(ab')2, Fv, Fab'-SH, F(ab')2, single chain antibodies, nanobodies, or scFv fragments. In some embodiments, one or both of the first and second antibodies or fragments further comprise an Fc domain. In some embodiments, the first antibody or fragment is a Fab fragment, and wherein the second antibody or fragment is a full-length antibody. In some embodiments, the first and the second antibodies or fragments are both full-length antibodies. In some embodiments, the first antibody or fragment is a Fab fragment coupled to monomeric streptavidin (mSA), and wherein the second antibody or fragment is a biotinylated full-length antibody. In some embodiments, the first antibody or fragment is a full-length antibody coupled to monomeric streptavidin (mSA), and wherein the second antibody or fragment is a biotinylated full-length antibody.

[0176] In some embodiments, an antibody or fragment is coupled to avidin, streptavidin, neutravidin, or a biotin-binding derivative thereof, or coupled to biotin or an avidin-binding derivative thereof, via a linker. Linkers for creating antibody fusion proteins are known in the art. In some embodiments, the linker comprises, consists of, or consists essentially of, glycine and/or serine residues. In some embodiments, the linker is 15-20 amino acids in length. In some embodiments, the linker comprises the sequence GGGSGGGSGGGS (SEQ ID NO:114). In some embodiments, the linker comprises one or more repeats of the sequence GGGGS (SEQ ID NO:115). In some embodiments, the linker comprises the sequence GGGGSGGGGSGGGGS (SEQ ID NO:116) or GGGGSGGGGSGGGGSGGGGS (SEQ ID NO:117). Additional linker sequences are described in Chen, X. *et al.* (2013) *Adv. Drug Deliv. Rev.* 65:1357-1369. In some embodiments (*e.g.,* in a scFv of the present disclosure), the scFv comprises one type of linker between the VH and VL domains, and another type of linker connecting the VL domain to the rest of the half-antibody, *e.g.*, to an Fc region. For example, in some embodiments, the linker between the VH and VL domains comprises glycine and/or serine residues, such as GGGSGGGSGGGS (SEQ ID NO:114), GGGGSGGGGSGGGGS (SEQ ID NO:116), GGGGSGGGGSGGGGSGGGGS (SEQ ID NO:117), or one or more repeats of the sequence GGGGS (SEQ ID NO:115); and/or the linker connecting the VL domain to the Fc region comprises EPKRSDKTHTCPPC (SEQ ID NO:118) or SATHTCPPC (SEQ ID NO:119). In some embodiments, the linker between the VH and VL domains comprises glycine and/or serine residues and is 15-20 amino acids in length.

[0177] In some embodiments, the first target of interest is human Dectin-1 (*e.g.*, isoform(s) A and/or B). In some embodiments, the second target of interest is a disease-causing agent. In some embodiments, the

second target of interest is human Dectin-1 (*e.g.*, isoform(s) A and/or B). In some embodiments, the first target of interest is a disease-causing agent.

[0178] In certain aspects, the present disclosure provides multispecific (*e.g.*, bispecific) antibodies and antibody fragments comprising at least one antigen binding domain that binds to human Dectin-1. Any of the antigen binding domains that bind to human Dectin-1 of the present disclosure may find use in a multispecific (*e.g.*, bispecific) binding molecule, antibody, or antibody fragment. In some embodiments, the multispecific (*e.g.*, bispecific) binding molecule, antibody, or antibody fragment further comprises at least one antigen binding domain that binds to a target of interest, *e.g.*, as described herein. In some embodiments, the target of interest is a disease-causing agent.

[0179] In some embodiments, the multispecific (*e.g.*, bispecific) binding molecule comprises a first antibody arm comprising an antibody heavy chain that comprises a first VH domain in association with an antibody light chain that comprises a first VL domain, and a first Fc region connected to the first VH domain, wherein the first and second VH domains form a first antigen-binding domain that binds to human Dectin-1, and a second antibody arm comprising an antibody heavy chain that comprises a VH domain in association with an antibody light chain that comprises a VL domain, and a second Fc region connected to the VH domain. That is, the first and second antibody arms can be of conventional antibody format (*see, e.g.,* **FIG. 67**).

[0180] Any of the VH and VL domains of the present disclosure that bind human Dectin-1 may find use in the first antibody arm. In some embodiments, the first VH domain comprises the amino acid sequence of SEQ ID NO: 209, and the first VL domain comprises the amino acid sequence of SEQ ID NO:210.

[0181] In some embodiments, the first VH domain comprises the amino acid sequence of SEQ ID NO: 213, and the first VL domain comprises the amino acid sequence of SEQ ID NO:214. In some embodiments, the first VH domain comprises the amino acid sequence of SEQ ID NO: 220, and the first VL domain comprises the amino acid sequence of SEQ ID NO:221. In some embodiments, the antibody heavy chain of the first antibody arm has a C→S amino acid substitution at position 5, according to IMGT hinge numbering; position 220, according to EU index; or position 233, according to Kabat numbering. Descriptions of the IMGT hinge, EU index, and Kabat numbering schemes are known in the art (*see, e.g.,* imgt.org/IMGTScientificChart/Numbering/Hu_IGHGnber.html), and therefore the precise location of this residue can be determined by the skilled person using knowledge common in the art. In some embodiments, the antibody heavy chain of the first antibody arm comprises the sequence ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSSDKTHTCPPCPAPELLGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSR EEMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG (SEQ ID NO:219). In some embodiments,

the antibody light chain of the first antibody arm has a C→S at the terminal residue of the light chain constant domain (*e.g.*, CK domain). In some embodiments, the antibody light chain of the first antibody arm comprises the sequence RADAAPTVSIFPPSSEQLTSGGASVVCFLNNFYPKDINVKWKIDGSERQNGVLNSWTDQ DSKDSTYSMSSTLTLTKDEYERHNSYTCEATHKTSTSPIVKSFNRNES (SEQ ID NO:223). In some embodiments, the first VH domain comprises the amino acid sequence of SEQ ID NO: 213; the first VL domain comprises the amino acid sequence of SEQ ID NO:214; the antibody heavy chain of the first antibody arm has a C→S amino acid substitution at position 5, according to IMGT hinge numbering; position 220, according to EU index; or position 233, according to Kabat numbering; and the antibody light chain of the first antibody arm has a C→S at the terminal residue of the light chain constant domain (*e.g.*, CK domain). In some embodiments, the first VH domain comprises the amino acid sequence of SEQ ID NO: 220; the first VL domain comprises the amino acid sequence of SEQ ID NO:221; the antibody heavy chain of the first antibody arm has a C→S amino acid substitution at position 5, according to IMGT hinge numbering; position 220, according to EU index; or position 233, according to Kabat numbering; and the antibody light chain of the first antibody arm has a C→S at the terminal residue of the light chain constant domain (*e.g.*, CK domain). In some embodiments, the first VH domain comprises the amino acid sequence of SEQ ID NO: 213; the first VL domain comprises the amino acid sequence of SEQ ID NO:214; the antibody heavy chain of the first antibody arm comprises the sequence of SEQ ID NO:219; and the antibody light chain of the first antibody arm comprises the sequence of SEQ ID NO:223. In some embodiments, the first VH domain comprises the amino acid sequence of SEQ ID NO: 220; the first VL domain comprises the amino acid sequence of SEQ ID NO:221; the antibody heavy chain of the first antibody arm comprises the sequence of SEQ ID NO:219; and the antibody light chain of the first antibody arm comprises the sequence of SEQ ID NO:223.

[0182] In some embodiments, the multispecific (*e.g.*, bispecific) binding molecule comprises a first antibody arm comprising a single chain variable fragment (scFv) comprising VH and VL domains of the present disclosure that bind to human Dectin-1 and a first Fc region, and a second antibody arm comprising an antibody heavy chain that comprises a VH domain in association with an antibody light chain that comprises a VL domain, and a second Fc region connected to the VH domain. In some embodiments, the scFv arm binds to Dectin-1, and the conventional antibody arm with VH and VL domains on separate polypeptides binds to a target of interest, *e.g.*, as described herein, such as a disease-causing agent. In some embodiments, the first Fc region comprises one or more knob-forming mutations, and the second Fc region comprises one or more cognate hole-forming mutations, or wherein the second Fc region comprises one or more knob-forming mutations, and the first Fc region comprises one or more cognate hole-forming mutations. In some embodiments, the first antibody arm comprises a first linker between the VH and VL domains (*e.g.*, of 15-20 amino acids in length), and a second linker between the VL domain and the first Fc region. In some embodiments, the first linker comprises one or more repeats of the sequence GGGGS (SEQ ID NO:115), *e.g.*, the sequence GGGGSGGGGSGGGGS (SEQ ID

NO:116) or GGGGSGGGGSGGGGSGGGGS (SEQ ID NO:117). In some embodiments, the second linker comprises the sequence EPKRSDKTHTCPPC (SEQ ID NO:118) or SATHTCPPC (SEQ ID NO:119). Additional linker sequences are described in Chen, X. *et al.* (2013) *Adv. Drug Deliv. Rev.* 65:1357-1369. A non-limiting example of this format is shown in **FIG. 51**.

[0183] In some embodiments, provided herein is a multispecific (*e.g.*, bispecific) binding molecule that comprises a first antibody arm comprising a single chain variable fragment (scFv) comprising VH and VL domains of the present disclosure that bind to human Dectin-1 and a first Fc region, and a second antibody arm comprising an antibody heavy chain that comprises a VH domain in association with an antibody light chain that comprises a VL domain and a second Fc region connected to the VH domain, wherein the VH and VL domains of the second antibody arm form an antigen binding domain that binds to a target of interest (*e.g.*, other than human Dectin-1). In some embodiments, the scFv of the first antibody arm comprises a VH domain that comprises the amino acid sequence of SEQ ID NO: 209, and a VL domain that comprises the amino acid sequence of SEQ ID NO:210. In some embodiments, the scFv of the first antibody arm comprises a VH domain that comprises the amino acid sequence of SEQ ID NO: 213, and a VL domain that comprises the amino acid sequence of SEQ ID NO:214. In some embodiments, the scFv of the first antibody arm comprises a VH domain that comprises the amino acid sequence of SEQ ID NO: 220, and a VL domain that comprises the amino acid sequence of SEQ ID NO:221. In some embodiments, the scFv of the first antibody arm comprises the amino acid sequence QVQLVQSGAEVKKPGASVKVSCKASGYTFTDYYMHWVRQAPGQGLEWMGWINPNEG DTNYAQKFEGRITMTRDTSISTAYMELSRLRSDDTAVYYCARNTGAYSFGYWGCGTLV TVSSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSVSASVGDRVTITCRASQGISSWLAW YQQKPGKCPKLLIYGASDLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQAYGFPF TFGPGTKVDIKEPK (SEQ ID NO:222). In some embodiments, the first antibody arm (including Fc region) comprises the amino acid sequence QVQLVQSGAEVKKPGASVKVSCKASGYTFTDYYMHWVRQAPGQGLEWMGWINPNEG DTNYAQKFEGRITMTRDTSISTAYMELSRLRSDDTAVYYCARNTGAYSFGYWGCGTLV TVSSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSVSASVGDRVTITCRASQGISSWLAW YQQKPGKCPKLLIYGASDLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQAYGFPF TFGPGTKVDIKEPKRSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCK VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPG (SEQ ID NO:224) or QVQLVQSGAEVKKPGASVKVSCKASGYTFTDYYMHWVRQAPGQGLEWMGWINPNEG DTNYAQKFEGRITMTRDTSISTAYMELSRLRSDDTAVYYCARNTGAYSFGYWGCGTLV

TVSSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSVSASVGDRVTITCRASQGISSWLAW YQQKPGKCPKLLIYGASDLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQAYGFPF TFGPGTKVDIKEPKRSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCK VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK (SEQ ID NO:225).

[0184] In some embodiments, the disease-causing agent is a bacterial cell, fungal cell, virus, senescent cell, tumor cell, protein aggregate, LDL particle, mast cell, eosinophil, ILC2 cell, or inflammatory immune cell. In some embodiments, the target of interest is an antigen expressed on the surface of the bacterial cell, fungal cell, senescent cell, tumor cell, mast cell, eosinophil, ILC2 cell, or inflammatory immune cell. In some embodiments, the target of interest is a surface antigen of the virus. In some embodiments, the target of interest is a protein aggregate or monomer thereof, *e.g.*, amyloid beta (such as in Alzheimer's disease), or lambda or kappa light chain amyloid (such as in light chain amyloidosis). In some embodiments, *e.g.*, for oncology applications, the second target of interest is CD70, HER2, DLL3, NECTIN-4, TROP-2, Mesothelin, LIV-1, C-MET, FOLR1, CD20, CCR8, CD33, or EGFR, *e.g.*, as expressed on the surface of a cancer cell.

[0185] In some embodiments, the target of interest is CD20, *e.g.*, human CD20. In some embodiments, the antigen binding domain that binds CD20 comprises a CDR-H1, CDR-H2, and CDR-H3 sequence from the VH domain sequence QVQLQQPGAELVKPGASVKMSCKASGYTFTSYNMHWVKQTPGRGLEWIGAIYPGNGDTSYNQ KFKGKATLTADKSSSTAYMQLSSLTSEDSAVYYCARSTYYGGDWYFNVWGAGTTVTVSA (SEQ ID NO:129) and/or a CDR-L1, CDR-L2, and CDR-L3 sequence from the VL domain sequence QIVLSQSPAILSASPGEKVTMTCRASSSVSYIHWFQQKPGSSPKPWIYATSNLASGVPVRFSGSGS GTSYSLTISRVEAEDAATYYCQQWTSNPPTFGGGTKLEIK (SEQ ID NO:130). In some embodiments, the antigen binding domain that binds CD20 comprises a VH domain that comprises the sequence QVQLQQPGAELVKPGASVKMSCKASGYTFTSYNMHWVKQTPGRGLEWIGAIYPGNGDTSYNQ KFKGKATLTADKSSSTAYMQLSSLTSEDSAVYYCARSTYYGGDWYFNVWGAGTTVTVSA (SEQ ID NO:129) and/or a VL domain that comprises the sequence QIVLSQSPAILSASPGEKVTMTCRASSSVSYIHWFQQKPGSSPKPWIYATSNLASGVPVRFSGSGS GTSYSLTISRVEAEDAATYYCQQWTSNPPTFGGGTKLEIK (SEQ ID NO:130). In some embodiments, the antigen binding domain that binds CD20 comprises the VH and VL domain sequences from rituximab. In some embodiments, the antigen binding domain that binds CD20 comprises the VH and VL domain sequences from obinituzumab. In some embodiments, the antigen binding domain that

binds CD20 comprises a VH domain that comprises the sequence of SEQ ID NO:137 and/or a VL domain that comprises the sequence of SEQ ID NO:138.

[0186] In some embodiments, provided herein is a multispecific (*e.g.*, bispecific) binding molecule that comprises a first antibody arm comprising a single chain variable fragment (scFv) comprising VH and VL domains of the present disclosure that bind to human Dectin-1 and a first Fc region, and a second antibody arm comprising an antibody heavy chain that comprises a VH domain in association with an antibody light chain that comprises a VL domain and a second Fc region connected to the VH domain, wherein the VH and VL domains of the second antibody arm form an antigen binding domain that binds to a target of interest (*e.g.*, a disease causing agent of the present disclosure). In some embodiments, the first Fc region comprises one or more knob-forming mutations, and the second Fc region comprises one or more cognate hole-forming mutations, or the second Fc region comprises one or more knob-forming mutations, and the first Fc region comprises one or more cognate hole-forming mutations. In some embodiments, the scFv comprises a first linker of the present disclosure between the VH and VL domains and a second linker of the present disclosure between the VL domain and the first Fc region.

[0187] In some embodiments, provided herein is a multispecific (*e.g.*, bispecific) binding molecule that comprises a first antibody arm comprising a single chain variable fragment (scFv) comprising VH and VL domains of the present disclosure that bind to human Dectin-1 and a first Fc region, and a second antibody arm comprising an antibody heavy chain that comprises a VH domain in association with an antibody light chain that comprises a VL domain and a second Fc region connected to the VH domain, wherein the VH and VL domains of the second antibody arm form an antigen binding domain that binds to CD20 (*e.g.*, human CD20). In some embodiments, the first Fc region comprises one or more knob-forming mutations, and the second Fc region comprises one or more cognate hole-forming mutations, or the second Fc region comprises one or more knob-forming mutations, and the first Fc region comprises one or more cognate hole-forming mutations. In some embodiments, the scFv comprises a first linker of the present disclosure between the VH and VL domains and a second linker of the present disclosure between the VL domain and the first Fc region.

[0188] In some embodiments, provided herein is a multispecific (*e.g.*, bispecific) binding molecule that comprises a first antibody arm comprising a single chain variable fragment (scFv) comprising VH and VL domains of the present disclosure that bind to human Dectin-1 and a first Fc region, and a second antibody arm comprising an antibody heavy chain that comprises a VH domain in association with an antibody light chain that comprises a VL domain and a second Fc region connected to the VH domain, wherein the VH and VL domains of the second antibody arm form an antigen binding domain that binds to HER2 (*e.g.*, human HER2). In some embodiments, the first Fc region comprises one or more knob-forming mutations, and the second Fc region comprises one or more cognate hole-forming mutations, or the second Fc region comprises one or more knob-forming mutations, and the first Fc region comprises one or more cognate hole-forming mutations. In some embodiments, the scFv comprises a first linker of the present disclosure between the VH and VL domains and a second linker of the present disclosure between

the VL domain and the first Fc region. In some embodiments, the second antibody arm comprises a VH domain comprising the sequence of EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPTNGYTRYADSV KGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYWGQGTLVTVSS (SEQ ID NO:131) and a VL domain comprising the sequence of DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLYSGVPSRFSGS RSGTDFTLTISSLQPEDFATYYCQQHYTTPPTFGQGTKVEIK (SEQ ID NO:132). In some embodiments, the antigen binding domain that binds HER2 comprises the VH and VL domain sequences from trastuzumab.

[0189] In some embodiments, provided herein is a multispecific (*e.g.*, bispecific) binding molecule that comprises a first antibody arm comprising a single chain variable fragment (scFv) comprising VH and VL domains of the present disclosure that bind to human Dectin-1 and a first Fc region, and a second antibody arm comprising an antibody heavy chain that comprises a VH domain in association with an antibody light chain that comprises a VL domain and a second Fc region connected to the VH domain, wherein the VH and VL domains of the second antibody arm form an antigen binding domain that binds to Trop-2 (*e.g.*, human Trop-2). In some embodiments, the first Fc region comprises one or more knob-forming mutations, and the second Fc region comprises one or more cognate hole-forming mutations, or the second Fc region comprises one or more knob-forming mutations, and the first Fc region comprises one or more cognate hole-forming mutations. In some embodiments, the scFv comprises a first linker of the present disclosure between the VH and VL domains and a second linker of the present disclosure between the VL domain and the first Fc region. In some embodiments, the second antibody arm comprises a VH domain comprising the sequence of QVQLQQSGSELKKPGASVKVSCKASGYTFTNYGMNWVKQAPGQGLKWMGWINTYTGEPTYTD DFKGRFAFSLDTSVSTAYLQISSLKADDTAVYFCARGGFGSSYWYFDVWGQGSLVTVSS (SEQ ID NO:139) and a VL domain comprising the sequence of DIQLTQSPSSLSASVGDRVSITCKASQDVSIAVAWYQQKPGKAPKLLIYSASYRYTGVPDRFSGSG SGTDFTLTISSLQPEDFAVYYCQQHYITPLTFGAGTKVEIK (SEQ ID NO:140). In some embodiments, the second antibody arm comprises a VH domain comprising the sequence of QIQLVQSGPELKKPGETVKISCKASGYTFTNYGMNWVKQAPGKGLKWMGWINTKTGEPTYAEE FKGRFAFSLETSASTAYLQINNLKKEDTATYFCGRGGYGSSYWYFDVWGAGTTVTVSS (SEQ ID NO:149) and a VL domain comprising the sequence of DIVMTQSHKFMSTSVGDRVSITCKASQDVSIAVAWYQQKPGQSPKVLIYSASYRYTGVPDRFTGS GSGTDFTFTISRVQAEDLAVYYCQQHYITPLTFGAGTKLELK (SEQ ID NO:150). In some embodiments, the second antibody arm comprises a VH domain comprising the sequence of QVQLQQSGPELVRPGTSVRISCKASGYTFTIYWLGWVKQRPGHGLEWIGNIFPGSAYINYNEKFK GKATLTADTSSSTAYMQLSSLTSEDSAVYFCAREGSNSGYWGQGTTLTVSS (SEQ ID NO:151) and a VL domain comprising the sequence of

DIVMTQSPSSLSVSAGEKVTMTCKSSQSLLNSGNQQNYLAWYQQKPGQPPKLLIYGASTRESGVP DRFTGSGSGTDFTLTINSVQAEDLAVYYCQSDHIYPYTFGGGTKLEIK (SEQ ID NO:152). In some embodiments, the second antibody arm comprises a VH domain comprising the sequence of QVQLQESGPGLVKPSETLSLTCTVSGGSISSYGVHWIRQPPGKGLEWIGVIWTGGSTDYNSALMS RVTISVDTSKNQFSLKLSSVTAADTAVYYCARDGDYDRYTMDYWGQGTLVTVSS (SEQ ID NO:153) and a VL domain comprising the sequence of DIVMTQSPDSLAVSLGERATINCRASKSVSTSGYSYMHWYQQKPGQPPKLLIYLASNLESGVPDR FSGSGSGTDFTLTISSLQAEDVAVYYCQHSRELPYTFGQGTKLEIK (SEQ ID NO:154). In some embodiments, the antigen binding domain that binds Trop-2 comprises the VH and VL domain sequences from sacituzumab, AR47A6.4.2, h7E6, or Pr1E11.

[0190] In some embodiments, provided herein is a multispecific (*e.g.*, bispecific) binding molecule that comprises a first antibody arm comprising a single chain variable fragment (scFv) comprising VH and VL domains of the present disclosure that bind to human Dectin-1 and a first Fc region, and a second antibody arm comprising an antibody heavy chain that comprises a VH domain in association with an antibody light chain that comprises a VL domain and a second Fc region connected to the VH domain, wherein the VH and VL domains of the second antibody arm form an antigen binding domain that binds to light chain amyloids (*e.g.*, human light chain amyloids, *e.g.*, human kappa light chain amyloids, human lambda light chain amyloids, or both human kappa and lambda light chain amyloids). In some embodiments, the first Fc region comprises one or more knob-forming mutations, and the second Fc region comprises one or more cognate hole-forming mutations, or the second Fc region comprises one or more knob-forming mutations, and the first Fc region comprises one or more cognate hole-forming mutations. In some embodiments, the scFv comprises a first linker of the present disclosure between the VH and VL domains and a second linker of the present disclosure between the VL domain and the first Fc region. In some embodiments, the second antibody arm comprises a VH domain comprising the sequence of QVQLKESGPGLVAPSQSLSITCTVSGFSLSSYGVSWVRQPPGKGLEWLGVIWGDGSTNYKPNLM SRLSISKDISKSQVLFKLNSLQTDDTATYYCVTLDYWGQGTSVTVSS (SEQ ID NO:143) and a VL domain comprising the sequence of DVVMTQTPLSLPVSLGDQASISCRSSQSLVHRNGNTYLHWYLQKPGQSPKLLIYKVSNRFSGVPD RFSGSGSGTDFTLKISRVEAEDLGLYFCFQTTYVPNTFGGGTKLEIK (SEQ ID NO:144). In some embodiments, the second antibody arm comprises a VH domain comprising the sequence of EVQLVESGGRLVQPKGSLKLSCAASGFTFNTYAMYWIRQAPGKGLEWVARIRSKSNNYAIYYAD SVKDRFTIFRDDSQSMLYLQMNNLKTEDTAMYYCVRPYSDSFAYWGQGTLVTVSA (SEQ ID NO:155) and a VL domain comprising the sequence of DVVMTQTPLSLPVSLGDQASISCRSSQSLVHSTGNTYLHWYLQKPGQSPKLLIYKVSNRFSGVPD RFSGSGSGTYFTLKISRVEAEDLGVYFCSQSTHVPFTFGGGTKLEIK (SEQ ID NO:156). In some embodiments, the second antibody arm comprises a VH domain comprising the sequence of EVQLVESGGRLVQPKGSLKLSCAASGFTFNTYAMYWIRQAPGKGLEWVARIRSKSNNYAIYYAD

SVKDRFTIFRDDSQSMLYLQMNNLKTEDTAMYYCVRPYSDSFAYWGQGTLVTVSA (SEQ ID NO:157) and a VL domain comprising the sequence of DVVMTQTPLSLPVSLGDQASISCRSSLSLVHSTGNTYLHWYLQKPGQSPKLLIYKVSNRFSGVPD RFSGSGSGTYFTLKISRVEAEDLGVYFCSQSTHVPFTFGGGTKLEIK (SEQ ID NO:158). In some embodiments, the antigen binding domain that binds light chain amyloid comprises the VH and VL domain sequences from antibody 11-1F4, 2A4, or 7D8.

[0191] In some embodiments, provided herein is a multispecific (*e.g.*, bispecific) binding molecule that comprises a first antibody arm comprising a single chain variable fragment (scFv) comprising VH and VL domains of the present disclosure that bind to human Dectin-1 and a first Fc region, and a second antibody arm comprising an antibody heavy chain that comprises a VH domain in association with an antibody light chain that comprises a VL domain and a second Fc region connected to the VH domain, wherein the VH and VL domains of the second antibody arm form an antigen binding domain that binds to amyloid beta (*e.g.*, human amyloid beta). In some embodiments, the first Fc region comprises one or more knob-forming mutations, and the second Fc region comprises one or more cognate hole-forming mutations, or the second Fc region comprises one or more knob-forming mutations, and the first Fc region comprises one or more cognate hole-forming mutations. In some embodiments, the scFv comprises a first linker of the present disclosure between the VH and VL domains and a second linker of the present disclosure between the VL domain and the first Fc region. In some embodiments, the second antibody arm comprises a VH domain comprising the sequence of QVQLVESGGGVVQPGRSLRLSCAASGFAFSSYGMHWVRQAPGKGLEWVAVIWFDGTKKYYTD SVKGRFTISRDNSKNTLYLQMNTLRAEDTAVYYCARDRGIGARRGPYYMDVWGKGTTVTVSS (SEQ ID NO:145) and a VL domain comprising the sequence of DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGS GTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIK (SEQ ID NO:146). In some embodiments, the second antibody arm comprises a VH domain comprising the sequence of EVQLVESGGGLVQPGGSLRLSCSASGFTFSSFGMHWVRQAPGKGLEWVAYISSGSSTIYYGDTV KGRFTISRDNAKNSLFLQMSSLRAEDTAVYYCAREGGYYYGRSYYTMDYWGQGTTVTVSS (SEQ ID NO:147) and a VL domain comprising the sequence of DVVMTQSPLSLPVTPGAPASISCRSSQSIVHSNGNTYLEWYLQKPGQSPKLLIYKVSNRFSGVPDR FSGSGSGTDFTLRISRVEAEDVGIYYCFQGSHVPPTFGPGTKLEIK (SEQ ID NO:148). In some embodiments, the antigen binding domain that binds amyloid beta comprises the VH and VL domain sequences from aducanumab or lecanemab.

[0192] In some embodiments, provided herein is a multispecific (*e.g.*, bispecific) binding molecule that comprises a first antibody arm comprising a single chain variable fragment (scFv) comprising VH and VL domains of the present disclosure that bind to human Dectin-1 and a first Fc region, and a second antibody arm comprising an antibody heavy chain that comprises a VH domain in association with an antibody light chain that comprises a VL domain and a second Fc region connected to the VH domain, wherein the

VH and VL domains of the second antibody arm form an antigen binding domain that binds to CD70 (*e.g.*, human CD70). In some embodiments, the first Fc region comprises one or more knob-forming mutations, and the second Fc region comprises one or more cognate hole-forming mutations, or the second Fc region comprises one or more knob-forming mutations, and the first Fc region comprises one or more cognate hole-forming mutations. In some embodiments, the scFv comprises a first linker of the present disclosure between the VH and VL domains and a second linker of the present disclosure between the VL domain and the first Fc region. In some embodiments, the second antibody arm comprises a VH domain comprising the sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFSVYYMNWVRQAPGKGLEWVSDINNEGGTTYYADS VKGRFTISRDNSKNSLYLQMNSLRAEDTAVYYCARDAGYSNHVPIFDSWGQGTLVTVSS (SEQ ID NO:133) and a VL domain comprising the sequence of QAVVTQEPSLTVSPGGTVTLTCGLKSGSVTSDNFPTWYQQTPGQAPRLLIYNTNTRHSGVPDRFS GSILGNKAALTITGAQADDEAEYFCALFISNPSVEFGGGTQLTVL (SEQ ID NO:134). In some embodiments, the antigen binding domain that binds CD70 comprises the VH and VL domain sequences from 4ID12.

[0193] In some embodiments, provided herein is a multispecific (*e.g.*, bispecific) binding molecule that comprises a first antibody arm comprising a single chain variable fragment (scFv) comprising VH and VL domains of the present disclosure that bind to human Dectin-1 and a first Fc region, and a second antibody arm comprising an antibody heavy chain that comprises a VH domain in association with an antibody light chain that comprises a VL domain and a second Fc region connected to the VH domain, wherein the VH and VL domains of the second antibody arm form an antigen binding domain that binds to nectin-4 (*e.g.*, human nectin-4). In some embodiments, the first Fc region comprises one or more knob-forming mutations, and the second Fc region comprises one or more cognate hole-forming mutations, or the second Fc region comprises one or more knob-forming mutations, and the first Fc region comprises one or more cognate hole-forming mutations. In some embodiments, the scFv comprises a first linker of the present disclosure between the VH and VL domains and a second linker of the present disclosure between the VL domain and the first Fc region. In some embodiments, the second antibody arm comprises a VH domain comprising the sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYNMNWVRQAPGKGLEWVSYISSSSSTIYYADSV KGRFTISRDNAKNSLSLQMNSLRDEDTAVYYCARAYYYGMDVWGQGTTVTVSS (SEQ ID NO:141) and a VL domain comprising the sequence of DIQMTQSPSSVSASVGDRVTITCRASQGISGWLAWYQQKPGKAPKFLIYAASTLQSGVPSRFSGS GSGTDFTLTISSLQPEDFATYYCQQANSFPPTFGGGTKVEIK (SEQ ID NO:142). In some embodiments, the second antibody arm comprises a VH domain comprising the sequence of QVQLKQSGPGLVQPSQSLSITCTVSGFSLTNYGVHWVRQSPGKGLEWLGVIWSGGSTDYNAAFIS RLSISKDTSKSQVFFKMNSLQADDTAIYYCARELIHAMDNWGQGTSVTVSS (SEQ ID NO:159) and a VL domain comprising the sequence of

DIQMTQSPASLSVSVGETVTITCRASENIYSNLAWYQQKQGNSPQLLVFAATNLADGVPSRFSGS GSGTQYSLKINSLQSEDFGTYYCQHFWGTPTFGGGTKLEIK (SEQ ID NO:160). In some embodiments, the antigen binding domain that binds nectin-4 comprises the VH and VL domain sequences from N41 or Ha22-2.

[0194] In some embodiments, provided herein is a multispecific (*e.g.*, bispecific) binding molecule that comprises a first antibody arm comprising a single chain variable fragment (scFv) comprising VH and VL domains of the present disclosure that bind to human Dectin-1 and a first Fc region, and a second antibody arm comprising an antibody heavy chain that comprises a VH domain in association with an antibody light chain that comprises a VL domain and a second Fc region connected to the VH domain, wherein the VH and VL domains of the second antibody arm form an antigen binding domain that binds to EGFR (*e.g.*, human EGFR). In some embodiments, the first Fc region comprises one or more knob-forming mutations, and the second Fc region comprises one or more cognate hole-forming mutations, or the second Fc region comprises one or more knob-forming mutations, and the first Fc region comprises one or more cognate hole-forming mutations. In some embodiments, the scFv comprises a first linker of the present disclosure between the VH and VL domains and a second linker of the present disclosure between the VL domain and the first Fc region. In some embodiments, the second antibody arm comprises a VH domain comprising the sequence of QVQLKQSGPGLVQPSQSLSITCTVSGFSLTNYGVHWVRQSPGKGLEWLGVIWSGGNTDYNTPFT SRLSINKDNSKSQVFFKMNSLQSNDTAIYYCARALTYYDYEFAYWGQGTLVTVSA (SEQ ID NO:161) and a VL domain comprising the sequence of DILLTQSPVILSVSPGERVSFSCRASQSIGTNIHWYQQRTNGSPRLLIKYASESISGIPSRFSGSGSGT DFTLSINSVESEDIADYYCQQNNNWPTTFGAGTKLELK (SEQ ID NO:162). In some embodiments, the second antibody arm comprises a VH domain comprising the sequence of QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGDYYWSWIRQPPGKGLEWIGYIYYSGSTDYNPSL KSRVTMSVDTSKNQFSLKVNSVTAADTAVYYCARVSIFGVGTFDYWGQGTLVTVSS (SEQ ID NO:163) and a VL domain comprising the sequence of EIVMTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPARFSGSG SGTDFTLTISSLEPEDFAVYYCHQYGSTPLTFGGGTKAEIK (SEQ ID NO:164). In some embodiments, the antigen binding domain that binds EGFR comprises the VH and VL domain sequences from cetuximab or necitumumab.

[0195] In some embodiments, provided herein is a multispecific (*e.g.*, bispecific) binding molecule that comprises a first antibody arm comprising a single chain variable fragment (scFv) comprising VH and VL domains of the present disclosure that bind to human Dectin-1 and a first Fc region, and a second antibody arm comprising an antibody heavy chain that comprises a VH domain in association with an antibody light chain that comprises a VL domain and a second Fc region connected to the VH domain, wherein the VH and VL domains of the second antibody arm form an antigen binding domain that binds to DLL3 (*e.g.*, human DLL3). In some embodiments, the first Fc region comprises one or more knob-forming

mutations, and the second Fc region comprises one or more cognate hole-forming mutations, or the second Fc region comprises one or more knob-forming mutations, and the first Fc region comprises one or more cognate hole-forming mutations. In some embodiments, the scFv comprises a first linker of the present disclosure between the VH and VL domains and a second linker of the present disclosure between the VL domain and the first Fc region. In some embodiments, the second antibody arm comprises a VH domain comprising the sequence of QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYGMNWVRQAPGQGLEWMGWINTYTGEPTYA DDFKGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARIGDSSPSDYWGQGTLVTVSS (SEQ ID NO:165) and a VL domain comprising the sequence of EIVMTQSPATLSVSPGERATLSCKASQSVSNDVVWYQQKPGQAPRLLIYYASNRYTGIPARFSGS GSGTEFTLTISSLQSEDFAVYYCQQDYTSPWTFGQGTKLEIK (SEQ ID NO:166). In some embodiments, the second antibody arm comprises a VH domain comprising the sequence of QVQLQESGPGLVKPSETLSLTCTVSGGSISSYYWSWIRQPPGKGLEWIGYVYYSGTTNYNPSLKS RVTISVDTSKNQFSLKLSSVTAADTAVYYCASIAVTGFYFDYWGQGTLVTVSS (SEQ ID NO:167) and a VL domain comprising the sequence of EIVLTQSPGTLSLSPGERVTLSCRASQRVNNNYLAWYQQRPGQAPRLLIYGASSRATGIPDRFSGS GSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTKLEIK (SEQ ID NO:168). In some embodiments, the antigen binding domain that binds DLL3 comprises the VH and VL domain sequences from rovalpituzumab or DLL3-4.

[0196] In some embodiments, provided herein is a multispecific (*e.g.*, bispecific) binding molecule that comprises a first antibody arm comprising a single chain variable fragment (scFv) comprising VH and VL domains of the present disclosure that bind to human Dectin-1 and a first Fc region, and a second antibody arm comprising an antibody heavy chain that comprises a VH domain in association with an antibody light chain that comprises a VL domain and a second Fc region connected to the VH domain, wherein the VH and VL domains of the second antibody arm form an antigen binding domain that binds to mesothelin (*e.g.*, human mesothelin). In some embodiments, the first Fc region comprises one or more knob-forming mutations, and the second Fc region comprises one or more cognate hole-forming mutations, or the second Fc region comprises one or more knob-forming mutations, and the first Fc region comprises one or more cognate hole-forming mutations. In some embodiments, the scFv comprises a first linker of the present disclosure between the VH and VL domains and a second linker of the present disclosure between the VL domain and the first Fc region. In some embodiments, the second antibody arm comprises a VH domain comprising the sequence of QVQLQQSGPELEKPGASVKISCKASGYSFTGYTMNWVKQSHGKSLEWIGLITPYNGASSYNQKF RGKATLTVDKSSSTAYMDLLSLTSEDSAVYFCARGGYDGRGFDYWGSGTPVTVSS (SEQ ID NO:169) and a VL domain comprising the sequence of DIELTQSPAIMSASPGEKVTMTCSASSSVSYMHWYQQKSGTSPKRWIYDTSKLASGVPGRFSGSG SGNSYSLTISSVEAEDDATYYCQQWSKHPLTFGSGTKVEIK (SEQ ID NO:170). In some

embodiments, the antigen binding domain that binds mesothelin comprises the VH and VL domain sequences from amatuximab.

[0197] In some embodiments, provided herein is a multispecific (*e.g.*, bispecific) binding molecule that comprises a first antibody arm comprising a single chain variable fragment (scFv) comprising VH and VL domains of the present disclosure that bind to human Dectin-1 and a first Fc region, and a second antibody arm comprising an antibody heavy chain that comprises a VH domain in association with an antibody light chain that comprises a VL domain and a second Fc region connected to the VH domain, wherein the VH and VL domains of the second antibody arm form an antigen binding domain that binds to CD33 (*e.g.*, human CD33). In some embodiments, the first Fc region comprises one or more knob-forming mutations, and the second Fc region comprises one or more cognate hole-forming mutations, or the second Fc region comprises one or more knob-forming mutations, and the first Fc region comprises one or more cognate hole-forming mutations. In some embodiments, the scFv comprises a first linker of the present disclosure between the VH and VL domains and a second linker of the present disclosure between the VL domain and the first Fc region. In some embodiments, the second antibody arm comprises a VH domain comprising the sequence of EVQLVQSGAEVKKPGSSVKVSCKASGYTITDSNIHWVRQAPGQSLEWIGYIYPYNGGTDYNQKF KNRATLTVDNPTNTAYMELSSLRSEDTAFYYCVNGNPWLAYWGQGTLVTVSS (SEQ ID NO:171) and a VL domain comprising the sequence of DIQLTQSPSTLSASVGDRVTITCRASESLDNYGIRFLTWFQQKPGKAPKLLMYAASNQGSGVPSRF SGSGSGTEFTLTISSLQPDDFATYYCQQTKEVPWSFGQGTKVEVK (SEQ ID NO:172). In some embodiments, the antigen binding domain that binds CD33 comprises the VH and VL domain sequences from gemtuzumab.

[0198] In some embodiments, provided herein is a multispecific (*e.g.*, bispecific) binding molecule that comprises a first antibody arm comprising a single chain variable fragment (scFv) comprising VH and VL domains of the present disclosure that bind to human Dectin-1 and a first Fc region, and a second antibody arm comprising an antibody heavy chain that comprises a VH domain in association with an antibody light chain that comprises a VL domain and a second Fc region connected to the VH domain, wherein the VH and VL domains of the second antibody arm form an antigen binding domain that binds to CCR8 (*e.g.*, human CCR8). In some embodiments, the first Fc region comprises one or more knob-forming mutations, and the second Fc region comprises one or more cognate hole-forming mutations, or the second Fc region comprises one or more knob-forming mutations, and the first Fc region comprises one or more cognate hole-forming mutations. In some embodiments, the scFv comprises a first linker of the present disclosure between the VH and VL domains and a second linker of the present disclosure between the VL domain and the first Fc region. In some embodiments, the second antibody arm comprises a VH domain comprising the sequence of EVQLVESGGRLVQPKGSLKLSCAASGFAFNTYALYWIRQAPGKGLEWVARIRSKSNNYATYYA DSVKDRFTISRDDSQSMLYLQMNNLKTEDTAMYYCVRARFYYSDYGYAMDYWGQGTSVTVSS

(SEQ ID NO:173) and a VL domain comprising the sequence of DIVMTQAAPSVPVTPGESVSISCRSSKSLLHSNGNTYLYWFLQRPGQSPQLLIYRMSNLASGVPDR FSGSGSGTAFTLRISRVEAEDVGVYYCMQHLEYPLTFGAGTKLELK (SEQ ID NO:174). In some embodiments, the antigen binding domain that binds CCR8 comprises the VH and VL domain sequences from 10A11.

[0199] In some embodiments, provided herein is a multispecific (*e.g.*, bispecific) binding molecule that comprises a first antibody arm comprising a single chain variable fragment (scFv) comprising VH and VL domains of the present disclosure that bind to human Dectin-1 and a first Fc region, and a second antibody arm comprising an antibody heavy chain that comprises a VH domain in association with an antibody light chain that comprises a VL domain and a second Fc region connected to the VH domain, wherein the VH and VL domains of the second antibody arm form an antigen binding domain that binds to CTLA4 (*e.g.*, human CTLA4). In some embodiments, the first Fc region comprises one or more knob-forming mutations, and the second Fc region comprises one or more cognate hole-forming mutations, or the second Fc region comprises one or more knob-forming mutations, and the first Fc region comprises one or more cognate hole-forming mutations. In some embodiments, the scFv comprises a first linker of the present disclosure between the VH and VL domains and a second linker of the present disclosure between the VL domain and the first Fc region. In some embodiments, the second antibody arm comprises a VH domain comprising the sequence of QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYTMHWVRQAPGKGLEWVTFISYDGNNKYYADS VKGRFTISRDNSKNTLYLQMNSLRAEDTAIYYCARTGWLGPFDYWGQGTLVTVSS (SEQ ID NO:175) and a VL domain comprising the sequence of EIVLTQSPGTLSLSPGERATLSCRASQSVGSSYLAWYQQKPGQAPRLLIYGAFSRATGIPDRFSGS GSGTDFTLTISRLEPEDFAVYYCQQYGSSPWTFGQGTKVEIK (SEQ ID NO:176). In some embodiments, the antigen binding domain that binds CTLA4 comprises the VH and VL domain sequences from ipilimumab.

[0200] In some embodiments, provided herein is a multispecific (*e.g.*, bispecific) binding molecule that comprises a first antibody arm comprising a single chain variable fragment (scFv) comprising VH and VL domains of the present disclosure that bind to human Dectin-1 and a first Fc region, and a second antibody arm comprising an antibody heavy chain that comprises a VH domain in association with an antibody light chain that comprises a VL domain and a second Fc region connected to the VH domain, wherein the VH and VL domains of the second antibody arm form an antigen binding domain that binds to cMET (*e.g.*, human cMET). In some embodiments, the first Fc region comprises one or more knob-forming mutations, and the second Fc region comprises one or more cognate hole-forming mutations, or the second Fc region comprises one or more knob-forming mutations, and the first Fc region comprises one or more cognate hole-forming mutations. In some embodiments, the scFv comprises a first linker of the present disclosure between the VH and VL domains and a second linker of the present disclosure between the VL domain and the first Fc region. In some embodiments, the second antibody arm comprises a VH

domain comprising the sequence of EVQLVESGGGLVQPGGSLRLSCAASGYTFTSYWLHWVRQAPGKGLEWVGMIDPSNSDTRFNPN FKDRFTISADTSKNTAYLQMNSLRAEDTAVYYCATYRSYVTPLDYWGQGTLVTVSS (SEQ ID NO:177) and a VL domain comprising the sequence of DIQMTQSPSSLSASVGDRVTITCKSSQSLLYTSSQKNYLAWYQQKPGKAPKLLIYWASTRESGVP SRFSGSGSGTDFTLTISSLQPEDFATYYCQQYYAYPWTFGQGTKVEIK (SEQ ID NO:178). In some embodiments, the antigen binding domain that binds cMET comprises the VH and VL domain sequences from onartuzumab.

[0201] In some embodiments, provided herein is a multispecific (*e.g.*, bispecific) binding molecule that comprises a first antibody arm comprising a single chain variable fragment (scFv) comprising VH and VL domains of the present disclosure that bind to human Dectin-1 and a first Fc region, and a second antibody arm comprising an antibody heavy chain that comprises a VH domain in association with an antibody light chain that comprises a VL domain and a second Fc region connected to the VH domain, wherein the VH and VL domains of the second antibody arm form an antigen binding domain that binds to LIV-1 (*e.g.*, human LIV-1). In some embodiments, the first Fc region comprises one or more knob-forming mutations, and the second Fc region comprises one or more cognate hole-forming mutations, or the second Fc region comprises one or more knob-forming mutations, and the first Fc region comprises one or more cognate hole-forming mutations. In some embodiments, the scFv comprises a first linker of the present disclosure between the VH and VL domains and a second linker of the present disclosure between the VL domain and the first Fc region. In some embodiments, the second antibody arm comprises a VH domain comprising the sequence of QVQLVQSGAEVKKPGASVKVSCKASGYTIEDYYMHWVRQAPGQGLEWMGWIDPENGDTEYAP TFQGRVTMTRDTSINTAYMELSRLRSDDTAVYYCARHDAHYGTWFAYWGQGTLVTVSS (SEQ ID NO:179) and a VL domain comprising the sequence of DVVMTQSPLSLPVTLGQPASISCRSSQSIIRNDGNTYLEWYQQRPGQSPRRLIYRVSNRFSGVPDR FSGSGSGTDFTLKISRVEAEDVGVYYCFQGSHVPYTFGGGTKVEIK (SEQ ID NO:180). In some embodiments, the antigen binding domain that binds LIV-1 comprises the VH and VL domain sequences from hLIV14.

[0202] In some embodiments, provided herein is a multispecific (*e.g.*, bispecific) binding molecule that comprises a first antibody arm comprising a single chain variable fragment (scFv) comprising VH and VL domains of the present disclosure that bind to human Dectin-1 and a first Fc region, and a second antibody arm comprising an antibody heavy chain that comprises a VH domain in association with an antibody light chain that comprises a VL domain and a second Fc region connected to the VH domain, wherein the VH and VL domains of the second antibody arm form an antigen binding domain that binds to ROR-1 (*e.g.*, human ROR-1). In some embodiments, the first Fc region comprises one or more knob-forming mutations, and the second Fc region comprises one or more cognate hole-forming mutations, or the second Fc region comprises one or more knob-forming mutations, and the first Fc region comprises one or

more cognate hole-forming mutations. In some embodiments, the scFv comprises a first linker of the present disclosure between the VH and VL domains and a second linker of the present disclosure between the VL domain and the first Fc region. In some embodiments, the second antibody arm comprises a VH domain comprising the sequence of QVQLQESGPGLVKPSQTLSLTCTVSGYAFTAYNIHWVRQAPGQGLEWMGSFDPYDGGSSYNQK FKDRLTISKDTSKNQVVLTMTNMDPVDTATYYCARGWYYFDYWGHGTLVTVSS (SEQ ID NO:181) and a VL domain comprising the sequence of DIVMTQTPLSLPVTPGEPASISCRASKSISKYLAWYQQKPGQAPRLLIYSGSTLQSGIPPRFSGSGY GTDFTLTINNIESEDAAYYFCQQHDESPYTFGEGTKVEIK (SEQ ID NO:182). In some embodiments, the antigen binding domain that binds ROR-1 comprises the VH and VL domain sequences from Ab1.

[0203] In some embodiments, provided herein is a multispecific (*e.g.*, bispecific) binding molecule that comprises a first antibody arm comprising a single chain variable fragment (scFv) comprising VH and VL domains of the present disclosure that bind to human Dectin-1 and a first Fc region, and a second antibody arm comprising an antibody heavy chain that comprises a VH domain in association with an antibody light chain that comprises a VL domain and a second Fc region connected to the VH domain, wherein the VH and VL domains of the second antibody arm form an antigen binding domain that binds to serum amyloid P (SAP), *e.g.*, human SAP. In some embodiments, the first Fc region comprises one or more knob-forming mutations, and the second Fc region comprises one or more cognate hole-forming mutations, or the second Fc region comprises one or more knob-forming mutations, and the first Fc region comprises one or more cognate hole-forming mutations. In some embodiments, the scFv comprises a first linker of the present disclosure between the VH and VL domains and a second linker of the present disclosure between the VL domain and the first Fc region. In some embodiments, the second antibody arm comprises a VH domain comprising the sequence of QVQLVQSGAEVKKPGSSVKVSCKASGFTFATYNMHWVRQAPGQGLEWMGYIYPGDGNANYN QQFKGRVTITADKSTSTAYMELSSLRSEDTAVYYCARGDFDYDGGYYFDSWGQGTLVTVSS (SEQ ID NO:183) and a VL domain comprising the sequence of DIQMTQSPSSLSASVGDRVTITCRASENIYSYLAWYQQKPGKAPKLLIHNAKTLAEGVPSRFSGSG SGTDFTLTISSLQPEDFATYYCQHHYGAPLTFGQGTKLEIK (SEQ ID NO:184). In some embodiments, the antigen binding domain that binds SAP comprises the VH and VL domain sequences from dezamizumab.

[0204] Multispecific antibodies have binding specificities for at least two different epitopes, usually from different antigens. Multispecific or bispecific antibodies can be prepared as full-length antibodies or antibody fragments (e.g., $F(ab')_2$ bispecific antibodies).

[0205] To enable the targeted removal of a disease-causing agent via phagocytosis, an antigen-binding domain of the present disclosure may be selected from IgGs, intrabodies, peptibodies, nanobodies, single

domain antibodies, SMTPs, and multispecific antibodies (e.g., bispecific antibodies, diabodies, triabodies, tetrabodies, tandem di-scFV, tandem tri-scFv, ADAPTIR).

[0206] Methods for making bispecific antibodies are known in the art. One well-established approach for making bispecific antibodies is the "knobs-into-holes" or "protuberance-into-cavity" approach. *See e.g.,* US Pat. No. 5,731,168. Two immunoglobulin polypeptides (*e.g.,* heavy chain polypeptides) each comprise an interface; an interface of one immunoglobulin polypeptide interacts with a corresponding or cognate interface on the other immunoglobulin polypeptide, thereby allowing the two immunoglobulin polypeptides to associate. In some embodiments, interfaces may be engineered such that a "knob" or "protuberance" located in the interface of one immunoglobulin polypeptide corresponds with a cognate "hole" or "cavity" located in the interface of the other immunoglobulin polypeptide. In some embodiments, a knob may be constructed by replacing a small amino acid side chain with a larger side chain. In some embodiments, a hole may be constructed by replacing a large amino acid side chain with a smaller side chain. Knobs or holes may exist in the original interface, or they may be introduced synthetically. Polynucleotides encoding modified immunoglobulin polypeptides with one or more corresponding knob- or hole-forming mutations may be expressed and purified using standard recombinant techniques and cell systems known in the art. See, e.g., U.S. Pat. Nos. 5,731,168; 5,807,706; 5,821,333; 7,642,228; 7,695,936; 8,216,805; 8,679,785; 8,844,834; U.S. Pub. No. 2013/0089553; Spiess et al., Nature Biotechnology 31: 753-758, 2013; and Ridgway and Carter (1996) Protein Eng. 9:617-621. Modified immunoglobulin polypeptides may be produced using prokaryotic host cells, such as *E. coli*, or eukaryotic host cells, such as mammalian cells (*e.g.*, CHO cells) or yeast cells. Corresponding knob- and hole-bearing immunoglobulin polypeptides may be expressed in host cells in co-culture and purified together as a heteromultimer, or they may be expressed in single cultures, separately purified, and assembled *in vitro*. Exemplary cognate knob and hole mutations are provided below (numbering according to EU index). EU numbering as used herein is known in the art; *see, e.g.,* IMGT resources at www.imgt.org/IMGTScientificChart/Numbering/Hu_IGHGnber.html and www.imgt.org/IMGTScientificChart/Numbering/Hu_IGKCnber.html. As used herein, an "antibody arm" may refer to the pairing between an antibody heavy chain and an antibody light chain, wherein the variable domains of the heavy and light chains form an antigen binding site that binds a target antigen.

Fc region 1	Y407T	Y407A	F405A	T394S	T366S L368A Y407V	T394W Y407T	T394S Y407A	T366W T394S
Fc region 2	T366Y	T366W	T394W	F405W	T366W	T366Y F405A	T366W F405W	F405W Y407A

[0207] According to a different approach, antibody variable domains with the desired binding specificities (antibody-antigen combining sites) are fused to immunoglobulin constant domain sequences.

[0208] In some embodiments, multispecific (*e.g.*, bispecific) antibodies further comprise one or more mutations on only one of the antibody arms to improve heavy chain/light chain pairing. For example, amino acid substitutions can be used to replace a native disulfide bond in the CH1-CL interface of one antibody arm with an engineered disulfide bond. *See, e.g.,* Mazor, Y. *et al.* (2015) *MAbs* 7:377-389 and EP3452089A2. In some embodiments, the multispecific or bispecific antibody comprises two antibody light chains and two antibody heavy chains, wherein only one of the antibody heavy chains comprises amino acid substitutions F126C and C220V, and only the corresponding or cognate light chain comprises amino acid substitutions S121C and C214V, according to EU numbering.

[0209] Multispecific (*e.g.*, bispecific) antibodies also include cross-linked or "heteroconjugate" antibodies. Techniques for generating bispecific antibodies from antibody fragments have also been described in the literature. For example, bispecific antibodies can be prepared using chemical linkage. In some embodiments, a bispecific antibody comprises a first IgG antibody comprising the first antigen binding domain covalently linked to a second IgG antibody comprising the second antigen binding domain.

[0210] In some embodiments, multispecific (*e.g.*, bispecific) antibodies further comprise one or more mutations on only one of the antibody arms to reduce binding affinity for Protein A. *See, e.g.,* Ollier, R. *et al.* (2019) *MAbs* 11:1464-1478 and AU2018204314. In some embodiments, the multispecific or bispecific antibody comprises two antibody light chains and two antibody heavy chains, wherein only one of the antibody heavy chains comprises amino acid substitutions H435R and Y436F, according to EU numbering.

[0211] In some embodiments, the monospecific or multispecific (*e.g.*, bispecific) antibodies further comprise one or more mutations to reduce effector function, *e.g.*, to reduce or eliminate binding of the Fc region to an Fc receptor. In some embodiments, the antibody comprises two antibody Fc regions, wherein the antibody Fc regions comprise an amino acid substitution at one or more of positions 234, 235, and 237, according to EU numbering. In some embodiments, the antibody comprises two antibody Fc regions, wherein the antibody Fc regions comprise L234A, L235E, and G237A substitutions, according to EU numbering.

[0212] In some embodiments, the monospecific or multispecific (*e.g.*, bispecific) antibodies comprise two antibody heavy chains and two antibody light chains, wherein the VH domain of the first antibody heavy chain forms an antigen binding domain with the VL domain of the first antibody light chain, wherein the VH domain of the second antibody heavy chain forms an antigen binding domain with the VL domain of the second antibody light chain, wherein the first antibody heavy chain comprises F126C, C220V, and T366W substitutions, wherein the first antibody light chain comprises S121C and C214V substitutions, and wherein the second antibody heavy chain comprises T366S, L368A, Y407V, H435R, and Y436F substitutions, according to EU numbering. In some embodiments, the first and second antibody heavy chains further comprise L234A, L235E, and G237A substitutions, according to EU

numbering. In some embodiments, the first and second antibody heavy chains comprise human IgG1 Fc domains.

[0213] In some embodiments, provided herein is a polynucleotide encoding the antibody or multispecific binding molecule of any one of the above embodiments. In some embodiments, provided herein is a vector (*e.g.*, an expression vector) comprising the polynucleotide of any one of the above embodiments. In some embodiments, provided herein is a host cell (*e.g.*, an isolated host cell or cell line) comprising the polynucleotide or vector of any one of the above embodiments. In some embodiments, provided herein is a pharmaceutical composition comprising the antibody or multispecific binding molecule of any one of the above embodiments and a pharmaceutically acceptable carrier. Any of these may find use in the methods of production and/or treatment disclosed herein.

[0214] In some embodiments, provided herein is a method of producing an antibody or multispecific binding molecule, comprising culturing the host cell of any one of the above embodiments under conditions suitable for production of the antibody or multispecific binding molecule. In some embodiments, the method further comprises recovering the antibody or multispecific binding molecule. The antibodies or multispecific binding molecules may be produced using standard recombinant techniques, as described herein, and/or as exemplified *infra*.

[0215] Antibodies and antibody fragments may be produced using recombinant methods. For example, nucleic acid encoding the antibody/fragment can be isolated and inserted into a replicable vector for further cloning or for expression. DNA encoding the antibody/fragment may be readily isolated and sequenced using conventional procedures (*e.g.*, via oligonucleotide probes capable of binding specifically to genes encoding the heavy and light chains of the antibody/fragment). Many vectors are known in the art; vector components generally include, but are not limited to, one or more of the following: a signal sequence, an origin of replication, one or more marker genes, an enhancer element, a promoter, and a transcription termination sequence. Suitable host cells for cloning or expressing the DNA in the vectors herein are the prokaryote, yeast, or higher eukaryote cells. When using recombinant techniques, the antibody/fragment can be produced intracellularly, in the periplasmic space, or directly secreted into the medium. If the antibody/fragment is produced intracellularly, the particulate debris, either host cells or lysed fragments, are removed, for example, by centrifugation or ultrafiltration. Where the antibody/fragment is secreted into the medium, supernatants from such expression systems are generally first concentrated using a commercially available protein concentration filter.

[0216] In some embodiments, an antibody or multispecific binding molecule of the present disclosure is part of a pharmaceutical composition, *e.g.*, including the antibody and one or more pharmaceutically acceptable carriers. Pharmaceutical compositions and formulations as described herein can be prepared by mixing the active ingredients (such as a fusion protein) having the desired degree of purity with one or more optional pharmaceutically acceptable carriers (*Remington's Pharmaceutical Sciences* 16th edition, Osol, A. Ed. (1980)), in the form of lyophilized formulations or aqueous solutions. Pharmaceutically acceptable carriers are generally nontoxic to recipients at the dosages and concentrations employed, and

include, but are not limited to: buffers such as phosphate, citrate, and other organic acids; antioxidants including ascorbic acid and methionine; preservatives; low molecular weight (less than about 10 residues) polypeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids; monosaccharides, disaccharides, and other carbohydrates including glucose, mannose, or dextrins; chelating agents such as EDTA; sugars such as sucrose, mannitol, trehalose or sorbitol; salt-forming counter-ions such as sodium; metal complexes (*e.g.* Zn-protein complexes); and/or non-ionic surfactants such as polyethylene glycol (PEG).

[0217] Certain aspects of the present disclosure relate to kits or articles of manufacture comprising any of the antibodies or multispecific binding molecules disclosed herein. In some embodiments, the article of manufacture comprises a container and a label or package insert on or associated with the container. In some embodiments, the kit or article of manufacture further comprises instructions for using the antibody or multispecific binding molecule according to any of the methods disclosed herein, *e.g.*, for treating a disease or disorder such as cancer.

[0218] Suitable containers include, for example, bottles, vials, syringes, etc. The containers may be formed from a variety of materials such as glass or plastic. The container holds a composition that is effective for treating the condition and may have a sterile access port (for example the container may be an intravenous solution bag or a vial having a stopper pierceable by a hypodermic injection needle). At least one active agent in the composition is an antibody or multispecific binding molecule as described herein. The label or package insert indicates that the composition is used for treating the particular condition. The label or package insert will further comprise instructions for administering the antibody or multispecific binding molecule composition to the subject. Articles of manufacture and kits comprising combinatorial therapies described herein are also contemplated.

II. Methods of Production and Identification

[0219] In certain aspects, the present disclosure provides methods of producing or generating multispecific (*e.g.*, bispecific) antibodies and antibody fragments. In some embodiments, the methods comprise providing a first antibody or antigen-binding fragment thereof comprising a first antigen-binding domain that binds to a first target of interest; providing a second antibody or antigen-binding fragment thereof comprising a second antigen-binding domain that binds to a second target of interest; and contacting the first antibody or fragment with the second antibody or fragment under conditions suitable for binding between the first antibody or fragment and the second antibody or fragment via an interaction between the avidin, streptavidin, neutravidin, or biotin-binding derivative thereof and the biotin or avidin-binding derivative thereof, thereby generating a multispecific binding molecule. In some embodiments, the first antibody or fragment is coupled to avidin, streptavidin, neutravidin, or a biotin-binding derivative thereof, and the second antibody or fragment is coupled to biotin or an avidin-binding derivative thereof. In some embodiments, the second antibody or fragment is coupled to avidin, streptavidin, neutravidin, or a biotin-binding derivative thereof, and the first antibody or fragment is coupled to biotin or an avidin-

binding derivative thereof. Any of the antigen binding domains, antibodies, and antibody fragments of the present disclosure (*e.g.*, as described *supra* in section I) may be produced or generated using the methods of producing or generating multispecific (*e.g.*, bispecific) antibodies and antibody fragments disclosed herein. Advantageously, this platform provides a modular format for generation of a variety of multispecific (*e.g.*, bispecific) binding molecules in which distinct antigen binding domains, antibodies, and/or antibody fragments are coupled together via a high affinity avidin: biotin interaction.

[0220] In certain aspects, the present disclosure provides methods of identifying a multispecific (*e.g.*, bispecific) binding molecule that binds a first and a second target of interest. In some embodiments, the methods comprise providing a first antibody or antigen-binding fragment thereof comprising a first antigen-binding domain that binds to a first target of interest; providing a second antibody or antigen-binding fragment thereof comprising a second antigen-binding domain that binds to a second target of interest; contacting the first antibody or fragment with the second antibody or fragment under conditions suitable for binding between the first antibody or fragment and the second antibody or fragment via an interaction between the avidin, streptavidin, neutravidin, or biotin-binding derivative thereof and the biotin or avidin-binding derivative thereof, thereby generating a multispecific binding molecule; and measuring binding between the multispecific binding molecule and at least one of the first and the second target of interest. In some embodiments, the first antibody or fragment is coupled to avidin, streptavidin, neutravidin, or a biotin-binding derivative thereof, and the second antibody or fragment is coupled to biotin or an avidin-binding derivative thereof. In some embodiments, the second antibody or fragment is coupled to avidin, streptavidin, neutravidin, or a biotin-binding derivative thereof, and the first antibody or fragment is coupled to biotin or an avidin-binding derivative thereof. Advantageously, this platform allows for screening a variety of antigen-binding domains for binding a target of interest in a multispecific (*e.g.*, bispecific) format.

[0221] In some embodiments, the first target of interest is human Dectin-1 (*e.g.*, isoform(s) A and/or B). In some embodiments, the second target of interest is a disease-causing agent. In some embodiments, the second target of interest is human Dectin-1 (*e.g.*, isoform(s) A and/or B). In some embodiments, the first target of interest is a disease-causing agent.

[0222] Any of the antigen binding domains, antibodies, and antibody fragments of the present disclosure (*e.g.*, as described *supra* in section I) may find use in the methods of identifying multispecific (*e.g.*, bispecific) antibodies and antibody fragments disclosed herein. In some embodiments, the antigen binding domains, antibodies, and antibody fragments bind to human Dectin-1. For example, in some embodiments, the antibody or fragment binds human Dectin-1 and is coupled to mSA via a linker.

[0223] Assays for measuring binding between the multispecific binding molecule and at least one of the first and the second target of interest are known in the art. In some embodiments, binding between the multispecific binding molecule and a purified antigen is measured, *e.g.*, as with an ELISA or SPR binding assay. In some embodiments, binding between the multispecific binding molecule and a cell expressing the antigen on its surface is measured, *e.g.*, as with a flow cytometry-based binding assay. In some

embodiments, binding between the multispecific binding molecule and a bead or other solid substrate coated with the antigen is measured. In some embodiments, a functional assay is used to detect an interaction between two or more cells (each expressing a surface antigen bound by an antigen binding domain of the multispecific binding molecule) brought together by binding the multispecific binding molecule, *e.g.*, by measuring cytokine production, cell death/phagocytosis, etc.

III. Methods of Use

[0224] In certain aspects, the present disclosure provides methods of treating a disease or disorder, comprising administering an effective amount of an antibody, antibody fragment, multispecific (*e.g.*, bispecific) binding molecule, or composition of the present disclosure to an individual in need thereof. In some embodiments, the individual is a human.

[0225] Any of the antigen binding domains, antibodies, and antibody fragments of the present disclosure (*e.g.*, as described *supra* in section I) may find use in the methods of treatment and uses disclosed herein, as well as the compositions (*e.g.*, pharmaceutical compositions) related thereto. For example, in some embodiments, the methods include using a multispecific (*e.g.*, bispecific) binding molecule of the present disclosure with a first antigen binding domain that binds to human Dectin-1, and a second antigen binding domain that binds to a disease-causing agent. In some embodiments, the disease-causing agent is a bacterial cell, fungal cell, virus, senescent cell, tumor cell, protein aggregate (*e.g.*, amyloid beta, or lambda or kappa light chain amyloids), LDL particle, mast cell, eosinophil, ILC2 cell, or inflammatory immune cell. In some embodiments, the target of interest is an antigen expressed on the surface of the bacterial cell, fungal cell, senescent cell, tumor cell, mast cell, eosinophil, ILC2 cell, or inflammatory immune cell. In some embodiments, the target of interest is a surface antigen of the virus. In some embodiments, the target of interest is CD70, HER2, DLL3, NECTIN-4, TROP-2, Mesothelin, LIV-1, C-MET, FOLR1, CD20, CCR8, CD33, or EGFR. Binding of the molecule that mediates targeted removal of a disease-causing agent via phagocytosis could be with and without avidity i.e., with and without inducing dimerization of the phagocytosis receptor such as Dectin-1 or the target antigen present on the agent.

[0226] In some embodiments, the disease or disorder is cancer, a bacterial infection, a fungal infection, a viral infection, a mast cell disease or disorder, systemic mastocytosis, amyloidosis, or an aging-related disease or disorder. There are variety of accumulated and not cleared aberrant host cells such as tumor, lymphoma, dead, necrotic, apoptotic, dying, infected, damaged cells that are associated with diseases. In addition, diverse cell products such as aggregated proteins (β-amyloid plaque, Tau aggregates, or antibody lambda or kappa light chain amyloids), lipoprotein particles, could cause a disease upon increased accumulation. Disease-causing cell may have glycoprotein, surface protein, or glycolipid typical of aberrant cells associated with a disease, disorder, or other undesirable condition. Besides the host generated agents, variety of foreign pathogens such as infectious microbes (e.g., viruses, fungus and bacteria) and the microbe generated products and debris (e.g., viral particle envelopes, endotoxin) may not

be well cleared in patients. In some embodiments, the virus is an influenza virus. In some embodiments, the virus is SARS-CoV-2.

[0227] The above listed abnormalities may cause illnesses such as cancer, Alzheimer disease, fibrosis, Parkinson disease, Huntington disease, HIV, Hepatitis A, B or C, sepsis etc. Many of these disorders or diseases are characterized by an accumulation of disease-causing agents in different organs in human subjects. In addition to the beneficial removal of a disease-causing agent via phagocytosis, the molecule may induce production of inflammatory mediators to alter the disease microenviroment such as in tumors, cancers and lymphomas. Without wishing to be bound to theory, it is thought that the molecule that performs targeted phagocytosis may demonstrate clear benefits for patients such as Alzheimer disease, Parkinson disease, cancer, infectious diseases (viral, bacterial, fungal, protozoan infections), inflammatory, or immune diseases (e.g., autoimmune diseases, inflammatory bowel diseases, multiple sclerosis), degenerative disease (e.g., joint and cartilage) Rheumatoid arthritis, Felty's syndrome, aggressive NK leukemia, IBM, IBD etc. In addition, targeted phagocytosis antibody treatment may have better activity of depleting cells in tissues over ADCC that relies on NK cells. The treatment may have a selective activity for removal of a particular disease-causing agent over a therapy that targets myeloid cells and improves phagocytosis in general. For example, targets of interest for treatment of cancer include, without limitation, CD70, HER2, DLL3, NECTIN-4, TROP-2, Mesothelin, LIV-1, C-MET, FOLR1, CD20, CCR8, CD33, and EGFR.

[0228] The following description is presented to enable a person of ordinary skill in the art to make and use the various embodiments. Descriptions of specific devices, techniques, and applications are provided only as examples. Various modifications to the examples described herein will be readily apparent to those of ordinary skill in the art, and the general principles defined herein may be applied to other examples and applications without departing from the spirit and scope of the various embodiments. Thus, the various embodiments are not intended to be limited to the examples described herein and shown, but are to be accorded the scope consistent with the claims.

EXAMPLES

Example 1: Functional characterization of 2M24 anti-Dectin-1 antibody

[0229] This example describes the production of monoclonal antibodies specific for human Dectin-1. This example also describes the characterization of a novel anti-human Dectin-1 antibody.

Materials and methods

Production of anti-Dectin-1 antibodies

[0230] Four-week-old, ATX-Gx transgenic mice were immunized subcutaneously with recombinant human Dectin-1 isoform B for five weeks, with one boost of antigen per week. Antibody titers in mouse

serum were assessed during pre- and post-boosts via ELISA and flow cytometry. The mice with the highest serum antibody titer were selected to supply B cells for the generation of hybridomas.

[0231] Prior to cell fusion, mice were administered with one additional boost of recombinant human Dectin-1 isoform B. Mice were sacrificed and the spleens were harvested. Spleen cells and SP2/0-Ag14 myeloma cells were mixed, in which fusion was then induced by 37 C incubation and in the presence of polyethylene glycol (PEG) or electroporation. The cells were then harvested and plated into 96 well plates with limited dilution to achieve one cell per well. The cells were subsequently treated with hypoxanthine, aminopterin and thymidine (HAT) medium and selected for over 2 weeks in culture.

[0232] To identify candidates specific towards Dectin-1, the hybridoma supernatants were screened by flow cytometry on cells overexpressing Dectin-1 and human primary monocytes. Cynomolgus monkey Dectin-1 cross-reactivity was assessed by antibody binding to cynomolgus monkey primary monocytes using flow cytometry.

Healthy donor samples

[0233] Fresh healthy donor buffy coats were obtained from Stanford Blood Center Peripheral blood mononuclear cells were isolated via ficoll paque (GE Healthcare, Chicago, IL) separation and cryopreserved in Bambanker cell freezing media (Bulldog Bio, Portsmouth, NH). Briefly, buffy coats were diluted in phosphate buffered saline (in 1:1 ratio), followed by layering of the diluted buffy coat in ficoll and centrifugation at 760 g. The PBMC layer was isolated and washed in PBS prior to downstream analysis Peripheral blood leukocytes were isolated through red blood cell lysis Cryopreserved cynomolgus monkey PBMC were obtained from Human Cells Biosciences.

Primary cells and cell culture

[0234] Human monocytes were isolated from healthy donor PBMCs according to the manufacturer's instructions of the pan monocyte isolation kit (Miltenyi Biotec, Inc., Auburn, CA) For macrophage and dendritic cells differentiation, monocytes were cultured in RPMI with 10 Human Serum (Millipore Sigma) in the presence of 50 ng/ml MCSF(Peprotech, Rocky Hill, NJ) for 6 days to fully differentiate into macrophages or in the presence of 50 ng/ml GMCSF and 50 ng/ml IL-4 (Peprotech, Rocky Hill, NJ) for 6 days to fully differentiate into dendritic cells. The medium with cytokines was refreshed every 3 days.

[0235] HEK Blue hDectin-1-a cells and HEK Blue hDectin-1-b cells (Invivogen, San Diego, CA) were maintained in DMEM/10% FBS supplemented with mormocin and puromycin according to manufacturer's instructions. Freestyle 293F cells were transiently transfected according to the manufacturer's suggestion (Thermo Fisher, Waltham, MA) Briefly, viable cell density and percent viability was determined Cells were diluted to a final density of 11×10^6 viable cells/mL with Freestyle 293 Expression Medium. Freestyle Max Reagent was diluted with OptiPro SFM Medium, mixed and incubated at room temperature for 5 minutes. The diluted Freestyle Max Reagent was added to plasmid

DNA diluted with OptiPro SFM Medium and mixed. The Freestyle Max Reagent/plasmid DNA complexes were incubated at room temperature for 10-20 minutes. The complexes were slowly transferred to the cells, swirling the culture flask gently during the addition, and the cells were then incubated in a 37 °C incubator with 80% relative humidity and 8% CO2 on an orbital shaker.

Binding of Dectin-1 antibodies to Dectin-1 expressing cells

[0236] Dectin-1 expressing cells (HEK Blue hDectin-1-a, HEK Blue hDectin-1-b, HEK293F hDectin-1 a FL, human monocytes or cyno monocytes) were plated at $1x10^5$-$2x10^5$ cells per well in non-tissue culture treated, 96 well V bottom plates. Additionally, human monocytes were incubated in human FcgR blocking antibody (Biolegend, San Diego, CA) for 10 minutes at room temperature to reduce binding of the antibodies to the Fc receptor. The cells were subsequently stained with the eFluor 506 viability dye (ThermoFisher, Waltham, MA) in a 1:1000 dilution for 30 minutes on ice, followed by a wash step in FACS buffer (PBS with 2% fetal bovine serum). Primary Dectin-1 antibodies or isotypes were used at a titration of 300, 100, 33.3, 11.1, 3.7, 1.23, 0.41, and 0.14 nM and incubated on ice for 30 minutes, followed by another wash step in FACS buffer.

[0237] For detection of mouse primary antibodies, the cells were incubated with a fluorescently labeled AF647 anti-mouse Fc-specific secondary antibody (Jackson Immuno). For detection of human IgG4 primary antibody, the cells were incubated for 30 minutes on ice with an Alexa Fluor 647 anti-human Fc-specific secondary antibody (Jackson Immuno) (detection in HEK cells) or a FITC anti-human IgG4 antibody (Sigma) (detection in primary monocytes). Data acquisition was performed using a CytoFlex flow cytometer (Beckman Coulter, Atlanta, GA) and analyzed using Graphpad Prism 8.4.

Dectin-1 antibody blocking of laminarin

[0238] HEK Blue hDectin-1a cells were plated at $1x10^5$ cells per well in non-tissue culture treated, 96 well V bottom plates. Primary anti-Dectin-1 antibodies were used at a titration of 300, 100, 33.3, 11.1, 3.7, 1.23, 0.41, 0.14, 0.05, 0.015 and 0.005 nM and incubated on ice for 30 minutes in the presence of 8 μ g/ml biotin laminarin. Following a wash step in FACS buffer, binding of biotin laminarin on the HEK cells was detected using streptavidin-AF647 for 30 minutes on ice. For analysis, 4000 cell events were acquired in a CytoFlex flow cytometer (Beckman Coulter, Atlanta, GA) and analyzed using Graphpad Prism 8.4.

Labelling of polysterene beads with pHrodo and conjugation to antibodies

[0239] Polystyrene beads of different sizes coated with goat anti-mouse IgG (or biotin) (Spherotech, Lake Forest, IL) were washed with PBS/Tween20 0.05% twice. pHrodo Red, succinimidyl ester (pHrodo Red, SE) (ThermoFisher, Waltham, MA) was added to the beads at 10 μ M and allowed to incubate for 60 minutes at room temperature with shaking. The beads were then washed with PBS/BSA 0.1% to remove excess pHrodo Red.

[0240] After pHrodo labeling, the antibody was conjugated to the beads according to the manufacturer's recommendations. Briefly, based on the binding capacity of the beads to antibody, an 5x excess of antibody was added to the beads and allowed to incubate at room temperature for 60 minutes with shaking. The beads were then washed with PBS/BSA 0.1% to remove unbound antibody. To assess the quality of the beads, pHrodo red activation was assessed in low pH buffer by flow cytometry. Antibody bound on the beads was assessed using a fluorescently labeled AF647 anti-mouse Fc specific or a FITC anti-human IgG4 antibody secondary antibody.

Antibody-dependent targeted phagocytosis of Phrodo labeled beads

[0241] For phagocytosis experiments, 50,000 HEK cells overexpressing Dectin-1 or primary cells (macrophages or dendritic cells) were seeded in a 96-well plate in RPMI with 10 ultra-low IgG FBS. pHrodo-labelled beads conjugated to anti-Dectin-1 antibodies or isotypes were added at a desired ratio ranging from 1:1 to 1:3 cells beads, and the plates were briefly spun down.

[0242] In some experiments cell tracker Calcein AM (Thermo Fisher, Waltham, MA) was added to label the cells. Phagocytosis was monitored in an IncuCyte S3 live imaging system (Germany) by taking images at desired time points and analyzed using the IncuCyte S3 software. Phagocytosis was quantified as the overlap of bright red fluorescence (engulfed beads) with Calcein AM positive cells or integrated red intensity of bright red fluorescence.

SEAP reporter assay in HEK cells overexpressing Dectin-1 with anti Dectin-1 antibodies

[0243] Anti-Dectin-1 monoclonal antibodies 2M24 (VH and VL domains comprising SEQ ID NO:62 and 64, respectively) or 15E2 and control isotypes were immobilized by coating onto the surfaces of wells of untreated 96-well, U bottomed polypropylene microtiter plates. For coating, 10, 2, 1, 0.5 and 0.1 μg of the anti-Dectin-1 antibody diluted in 50 μl sterile PBS was added to each well. Plates were left overnight in a class II laminar flow cabinet with the lids removed to allow the solutions to evaporate. Coated plates were washed twice with 200 μl sterile PBS to remove salt crystals and unbound antibody. HEK Blue hDectin-1-a cells were then cultured on the plates in RPM1 with 10% ultra-low IgG FBS (VWR)for 22 hours and alkaline phosphatase levels were assessed in the supernatant at OD 630 nm using QUANTI Blue Solution (Invivogen, San Diego, CA) per manufacturer's instructions.

[0244] To determine HEK cells SEAP secretion induced by anti-Dectin-1 antibody conjugated beads, streptavidin-2M24 (hIgG4) was conjugated to biotin polystyrene beads of 3, 10 and 16 μm in size (Spherotech, Lake Forest, IL) by incubating the beads with the antibody for 30 minutes in room temperature and washing twice with PBS to remove the unbound antibody. Anti-Dectin-1 antibody-conjugated beads were mixed with $1x10^5$ HEK Blue hDectin-1-a cells at a ratio of 1:3 cells: bead in RPM1 with 10% ultra-low IgG FBS for 22 hours, followed by evaluation of alkaline phosphatase secretion at OD 630 nm in the supernatant as described above.

Cytokine secretion

[0245] Anti-Dectin-1 monoclonal antibodies 2M24 or 15E2 clones and control isotypes were immobilized by coating 10 ug onto the surfaces of wells of untreated 96-well, U bottomed polypropylene microtiter plates as described above. Freshly isolated monocytes or peripheral blood mononuclear cells were then cultured on the plates with the immobilized antibodies in RPM1 with 10% ultra-low IgG FBS at 200,000 cell/per well for 24 hours. In other wells the cells were treated with 10 μ g/ml of Dectin-1 antibodies in solution instead of immobilized antibodies. TNFa, IL-6 and IFNg in the supernatant were assessed using the U-PLEX Assay Platform (Meso Scale Discovery) and their levels were expressed as fold change of Dectin-1 antibody-induced cytokine secretion versus the isotype control. As a positive control, cells were stimulated with zymosan at 25 μ g/ml.

Results

[0246] To generate Dectin-1 antibodies, four-week-old, ATX-Gx Alloy transgenic mice were immunized subcutaneously with recombinant Dectin-1 isoform B protein, with one boost of antigen per week. The antibodies generated from this immunization have a human variable domain and a mouse constant domain.

[0247] From the 56 candidate anti-Dectin-1 antibody clones generated in this study, the 2M24 clone was the only one that showed binding to both Dectin-1 isoforms A and B in HEK cells as well as to monocytes. As shown in **FIG. 1A**, the 2M24 anti-Dectin-1 antibody clone demonstrated high affinity to Dectin-1 expressing human monocytes. In contrast, other clones bound only to Dectin-1 isoform A (e.g., 2M08, 2M12, 2M38) or showed no binding at all (2M49). Moreover, the affinity to Dectin-1 of2M24 was superior to the affinity presented by other clones and the commercial Dectin-1 antibodies (15E2, 259931, GE2). **FIG. 1C** shows a comparison of the binding to human monocytes and HEK cells overexpressing Dectin-1 between 2M24 clone and other Dectin-1 clones identified from the Alloy transgenic mice immunization, as well as commercial Dectin-1 clones.

[0248] The 2M24 antibody was also assessed for its cross-reactivity to cynomolgus Dectin-1. The binding was assessed by flow cytometry analysis of cynomolgus monkey monocytes derived from PBMCs. As shown in **FIG. 1B**, anti-human Dectin-1 clone 2M24 antibody demonstrated cross-reactivity and high affinity to cynomolgus monkey Dectin-1 expressed on monocytes. The 2M24 anti-Dectin-1 antibody was superior to commercial antibodies tested in terms of affinity, exhibiting an EC50 of 0.3 nM. The agonistic 15E2 and the 255931 commercial antibodies exhibited EC50 of 14 nM and16 nM, respectively, in cynomolgus monkey monocytes. **FIG. 1C** shows a comparison of binding to cynomolgus monkey monocytes between 2M24 clone and the commercial clones 15E2 and 259931.

[0249] To assess the functionality of the 2M24 Dectin-1 antibody in promoting phagocytosis, polystyrene beads were coated with the 2M24 antibody and mixed with HEK-Blue hDectin-1a cells or primary human monocytes. The 2M24 antibody efficiently induced the phagocytosis of the beads. As

shown in **FIGs. 2A-2B**, the 2M24 anti-Dectin-1 antibody coupled to polystyrene beads promoted phagocytosis in both HEK-Blue hDectin-1a cells and human primary monocytes.

[0250] From the mIgG1 2M24 clone, a fully human 2M24 antibody of the IgG4 isotype was developed. This antibody has human constant and variable regions. The functionality of the hIgG4 2M24 was then assessed for binding to two Dectin-1 expressing cell types, HEK-Blue hDectin-1a cells and human monocytes. As shown in **FIGs. 3A-3B**, the fully human 2M24 showed high affinity binding to Dectin-1 in transfected HEK cells (EC50 = 1.6 nM) and human monocytes (EC50 = 0.7 nM).

[0251] Next, the hIgG4 2M24 antibody was tested for its ability to promote phagocytosis of beads in Dectin-1 expressing cells. As shown in **FIG. 4**, the hIgG4 2M24 antibody exhibited efficient phagocytic ability in HEK cells overexpressing Dectin-1, human monocytes, and human macrophages. Thus, the fully human IgG4 2M24 antibody can promote phagocytosis in Dectin-1 expressing cells.

[0252] The fully human 2M24 (hIgG4) anti-Dectin-1 antibody was also tested for its ability to promote signaling through Dectin-1. Activation of Dectin-1 signaling by the antibodies can be assessed with a secreted alkaline phosphatase assay using HEK-Blue hDectin-1a cells. The HEK-Blue hDectin-1a cells have been engineered to express Dectin-1 isoform A and genes involved in the Dectin-1/NF-κB/SEAP signaling pathway and thus express a secreted alkaline phosphatase (SEAP) in response to stimulation by Dectin-1 ligands. As shown in **FIGs. 5A-5B**, the 2M24 (hIgG4) anti-Dectin-1 antibody induced alkaline phosphatase secretion in HEK-Blue hDectin-1a cells both in immobilized form and conjugated to beads. These observations support the idea that the 2M24 (hIgG4) antibody promotes SEAP secretion by engaging Dectin-1 on the surface of the cells, indicating clustering of the receptor and an agonistic activity by this antibody. Moreover, efficient clustering signaling of Dectin-1 can be promoted by beads conjugated to 2M24 (hIgG4). Signaling was better induced with bigger beads, reflecting better clustering of the receptor. This supports that clustering of Dectin-1 promoted by a bispecific antibody comprising the anti-Dectin-1 antibody, which targets a phagocyte, and an antibody targeting another cell, such as a cancer cell, could promote clustering and signaling by Dectin-1 on the phagocyte.

[0253] Natural ligands of Dectin-1 cluster the receptor and signal downstream of Dectin-1/Syk/NFkB to induce inflammatory gene expression. To assess if engagement of Dectin-1 antibody in solution can trigger cytokine secretion, monocytes or macrophages were treated with 10 ug/ml of a commercial anti-Dectin-1 antibody. As shown in **FIGs. 6A-6B**, the 15E2 commercial anti-Dectin-1 antibody did not induce cytokine secretion in primary human macrophages and monocytes, indicating that there was insufficient clustering of the Dectin-1 receptor. This data supports that free Dectin-1 antibody in solution does not induce immunostimulation, due to lack of sufficient Dectin-1 clustering.

[0254] To assess if cytokine secretion could be induced by the 2M24 (hIgG4) anti-Dectin-1 antibody, the antibody was immobilized on beads and cultured with monocytes or PBMCs. As shown in **FIGs. 7A-7B**, the 2M24 anti-Dectin-1 antibody induced cytokine secretion in primary human monocytes and PBMCs. The 2M24 antibody not only promoted cytokine secretion, but also exhibited superior immunostimulation as compared to that promoted by the 15E2 anti-Dectin-1 agonistic antibody. Of the

cytokines measured in this experiment, TNFa and IL6 are secreted by monocytes that express Dectin-1. In contrast, IFNg is mainly secreted by T-cells that exist in PBMCs. Because T-cells do not express Dectin-1, they are not activated directly by the anti-Dectin-1 antibodies, but rather from cytokines secreted by the monocytes in the PBMCs that are stimulated by the Dectin-1 antibodies. The differential effect of Dectin-1 antibodies on IFNg was therefore more prominent in PBMCs than in pure monocytes.

[0255] Finally, the activation of Dectin-1 by natural ligands in the presence of anti-Dectin-1 antibody was tested. HEK-Blue hDectin-1a cells were incubated in a 1/3 serial dose titration of 2M24 (hIgG4) Dectin-1 antibody or the 15E2, 259931, GE2 anti-Dectin-1 commercial antibodies starting at 300 nM in the presence of 8 ug/ml of biotinylated laminarin. As shown in **FIG. 8**, binding of the 2M24 (hIgG4) antibody to Dectin-1 did not block the binding of laminarin, a natural ligand of Dectin-1. Thus, engaging Dectin-1 with the 2M24 anti-Dectin-1 antibody does not block clearance of pathogens and is unlikely to increase susceptibility to potential fungal infections.

[0256] In conclusion, the 2M24 anti-Dectin-1 antibody can induce phagocytosis by Dectin-1 expressing cells and can induce activation of Dectin-1 signaling without competing with the natural ligands for Dectin-1. The properties of the 2M24 and 15E2 antibodies are summarized in **FIG. 9**.

Example 2: Bispecific anti-Dectin-1 antibodies

[0257] This example describes the generation and characterization of bispecific antibodies comprising a Dectin-1-binding arm and a second arm that binds specific tumor antigens.

Materials and Methods

Generation of bispecifics

[0258] Antibodies were differentially labeled with MTA or FOL reagent following manufacturer's guidelines (AAT Bioquest). Labeled antibodies were mixed and incubated to allow for covalent assembly via MTA and FOL interaction. The following antibodies were used for bioin: streptavidin-induced bispecific antibodies:

Anti-Dectin-1 15E2 antibody heavy chain: mSA fusion
QWQLQQSGAELARPGASWKMSCKASGYTFTTYTMHWWKQRPGQGLEWIGYINPSSGYTNYNQ
KFKDKATLTADKSSSTASMQLSSLTSEDSAWYYCARERAVLVPYAMDYWGQGTSVTVSSASTK
GPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVT
VPSSSLGTKTYTCNVDHKPSNTKVDKRVGGGSGGGSGGGSEFASAEAGITGTWYNQHGSTFTVT
AGADGNLTGQYENRAQGTGCQNSPYTLTGRYNGTKLEWRVEWNNSTENCHSRTEWRGQYQG
GAEARINTQWNLTYEGGSGPATEQGQDTFTKVKPSAASGSAAAGASHHHHHH (SEQ ID NO:121)

Anti-Dectin-1 15E2 antibody light chain

QIVLTQSPAVMSASPGEKWTITCTASSSLSYMHWFQQKPGTSPKLWLYSTSILASGVPTRFSGSGS
GTSYSLTISRMEAEDAATYYCQQRSSSPFTFGSGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVC
LLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVT
HQGLSSPVTKSFNRGEC (SEQ ID NO:122)

Avi-tagged anti-CD20 Fab heavy chain (CH1 domain based on hIgG4 sequence)
QVQLQQPGAELVKPGASVKMSCKASGYTFTSYNMHWVKQTPGRGLEWIGAIYPGNGDTSYNQ
KFKGKATLTADKSSSTAYMQLSSLTSEDSAVYYCARSTYYGGDWYFNVWGAGTTVTVSAASTK
GPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVT
VPSSSLGTKTYTCNVDHKPSNTKVDKRVAAAGASHHHHHHGSGLNDIFEAQKIEWHE (SEQ ID
NO:123)

Anti-CD20 Fab light chain
QIVLSQSPAILSASPGEKVTMTCRASSSVSYIHWFQQKPGSSPKPWIYATSNLASGVPVRFSGSGS
GTSYSLTISRVEAEDAATYYCQQWTSNPPTFGGGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVV
CLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVT
HQGLSSPVTKSFNRGEC (SEQ ID NO:124)

Avi-tagged anti-HER2 Fab heavy chain (CH1 domain based on hIgG4 sequence)
EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPTNGYTRYADSV
KGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYWGQGTLVTVSSASTKGPS
VFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPS
SSLGTKTYTCNVDHKPSNTKVDKRVAAAGASHHHHHHGSGLNDIFEAQKIEWHE (SEQ ID
NO:125)

Anti-HER2 Fab light chain
DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLYSGVPSRFSGS
RSGTDFTLTISSLQPEDFATYYCQQHYTTPPTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASV
VCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACE
VTHQGLSSPVTKSFNRGEC (SEQ ID NO:126)

Cell coupling assay

[0259] Dectin-1-expressing cells were labelled with calcein green, and target cells were labelled with calcein reds. The cells were incubated in the presence of a bispecific or an isotype control antibody, then analyzed by flow cytometry. Coupling of the cells was indicated by a double positive signal (green+red+). Coupling efficiency was quantified as the percentage of total target cells that forms doublets with Dectin-1-expressing cells.

[0260] Five million effector (Dectin-1 expressing cells) or target cells (cells expressing the target of interest, *e.g.*, CD20 positive Raji cells or HER2 positive SKBR3 cells) were differentially labeled with either calcein green (0.5nM) or calcein red/pHrodo-red (0.5 nM). Cells were thoroughly washed with PBS and kept on ice. Effector and target cells were then co-cultured at a 3:1 ratio (effector: target) in the presence of 2M24 bispecific antibody or isotype control and incubated for 30 minutes at 37°C. Following incubation, samples were gently resuspended and analyzed by flow cytometry. PMT voltages were adjusted accordingly, and cells were gated based on FITC and/or PE fluorescence corresponding to calcein green or red fluorescence. Coupling efficiency is reported as the number of PE-positive cells (target cells) in the doublet population, divided by the total number of PE-positive target cells in the reaction.

SEAP reporter assay in HEK cells overexpressing Dectin-1 with anti Dectin-1 antibodies

[0261] To determine HEK cell SEAP secretion induced by Raji cells (expressing CD20), Raji cells were coated with a 2M24/anti-hCD20 or a hIgG4 /anti-CD20 bispecific for 30 minutes on ice, followed by washing twice with PBS to remove the unbound bispecific. The bispecific-coated Raji cells were mixed with $1x10^5$ HEK Blue hDectin-1-a cells at a ratio of 1:2 (HEK cells Raji cells) in RPM1 with 10% ultra-low IgG FBS. After 22 hours, alkaline phosphatase secretion in the supernatant was evaluated at OD 630 nm as described in Example 2.

Results

[0262] Dectin-1 agonist bispecific antibodies can exploit various modes of activity (e.g., immune activation, phagocytosis, neoantigen presentation and adaptive immunity activation) for the targeted depletion of cancer cells (**FIGs. 11A-11B**). As a proof-of-concept to engage a Dectin-1 antibody (15E2 or 2M24) and a target antibody, a click-chemistry approach was used to develop bispecifics comprising an anti-Dectin-1-targeting arm and a second arm targeting a protein of interest. This approach enabled the generation of bispecifics for various assays. A schematic of this approach is shown in **FIGs. 10A-10B**. As binding of Dectin-1 by Dectin-1-specific antibodies can induce phagocytosis of targets (see Example 1 and Example 2), the bispecific antibodies were evaluated for their ability to promote phagocytosis of specific target cells. First, the bispecifics were evaluated for their ability to eliminate CD70-expressing cancer cells by phagocytosis. CD70 is a type II transmembrane glycoprotein that belongs to the tumor necrosis factor (TNF) superfamily. CD70 is expressed at low levels in normal tissues, but is highly overexpressed in various diseases, including acute myeloid leukemia (AML), renal cell carcinoma, rheumatoid arthritis and lupus.

[0263] Using click chemistry, a bispecific molecule comprising a Dectin-1-targeting arm (anti-Dectin-1; clone 2M24) and a CD70-targeting arm (anti-hCD70; clone 113-16) was generated. The purity of the bispecific (2M24/anti-hCD70) antibody was assessed by SDS-PAGE analysis (**FIG. 12A**), while binding was assessed by flow cytometry analysis (**FIG. 12B**). As shown in **FIG. 12B**, binding studies on cells

revealed that 2M24/anti-hCD70 bound to the HEK293 cell line expressing Dectin-1 with an EC50 of 1.8 nM and bound to CD70-positive renal carcinoma cell lines with an EC50 of 12.34 nM (A498 cells) or 11.62 nM (786-0 cells). The bispecific was then evaluated for its ability to induce cell coupling. As shown in **FIG. 13**, the 2M24/anti-hCD70 bispecific induced coupling of Dectin-1-expressing HEK293 cells and CD70-expressing renal carcinoma cells, resulting in cell doublets of HEK293 cells (labeled with calcein green) and A498 cells (labeled with calcein red).

[0264] Next, targeting of CD20-expressing cells with a bispecific was evaluated. CD20 is a transmembrane protein present on virtually all B cells from the stage at which they become committed to B-cell development until it is downregulated when they differentiate into antibody-secreting plasma cells and is considered a pan-B-cell antigenic marker. As shown in **FIGs. 14A-14B**, a 2M24/anti-hCD20 bispecific induced coupling of Dectin-1-expressing cells (both Dectin-1-expressing HEK293 cells and human M0 macrophages) with CD20-expressing B cells (Raji cell line). This cell-to-cell coupling mediated by the bispecific could induce synapse formation between effector and target cell that may alter cytokine signaling, activate phagocytosis and ultimately target antigen presentation.

[0265] To test for induction of signaling resulting from stimulation with bispecific antibodies that bind Dectin-1, a secreted alkaline phosphatase assay was performed. As shown in **FIG. 15**, Raji cells coated with an anti-Dectin-1/anti-CD20 bispecific induced alkaline phosphatase secretion in HEK-Blue hDectin-1a cells. Thus, using a bispecific antibody to connect a target cell with a cell expressing Dectin-1 (such as phagocyte) can promote signaling by the Dectin-1 expressing cell. In the case of phagocytes, signaling may result in the production of cytokines and immunostimulation.

[0266] Previously, it was demonstrated that Dectin-1 expression in HEK 293 cells is necessary and sufficient to induce phagocytosis of various size beads coated with anti-Dectin-1 targeting antibody (see Example 1 and Example 2). To demonstrate phagocytosis of live target cells, a bispecific comprising an Dectin-1-targeting arm and a CD20-targeting arm was developed. In a co-culture assay of HEK 293 cells and CD20-expressing Raji cells, phagocytosis in cells treated with anti-Dectin-1/anti-hCD20 bispecific was observed, in contrast to isotype control bispecifics (**FIG. 16**). Furthermore, pre-incubation of cells with Latrunculin A, an inhibitor of phagocytosis that blocks actin polymerization, blocked phagocytosis of cells treated with anti-Dectin-1/anti-hCD20 bispecific. These findings indicate that Dectin-1 expression is sufficient to induce phagocytosis, and that co-targeting Dectin-1 and a target of interest with an Dectin-1-agonistic bispecific is sufficient to induce phagocytosis of a target cell.

[0267] A proof-of-concept experiment was performed for co-targeting Dectin-1-expressing cells and HER2-positive breast cancer cells using an anti-Dectin-1/anti-HER2 bispecific antibody. Approximately 20% to 25% of invasive breast cancers exhibit overexpression of the human epidermal growth factor receptor HER2 tyrosine kinase receptor. As shown in **FIG. 17**, anti-Dectin-1 (15E2)/anti-HER2 bispecific induced coupling of Dectin-1- and HER2-expressing cells. This interaction is thought to promote synapse formation between effector and target cells, as Dectin-1 clustering induces cytokine

secretion by effector cells, triggers phagocytosis of target cells, and leads to neo-antigen presentation and activation of adaptive immune cells (B and T cells).

[0268] Finally, an anti-Dectin-1 (2M24)/anti-hCD94 bispecific was also evaluated. Large granular lymphocyte (LGL) leukemia is a rare chronic lymphoproliferative disease of T cell and natural killer (NK) cell lineage. CD94/NKG2 is a family of C-type lectin receptors which are expressed predominantly on the surface of NK cells and a subset of CD8+ T-lymphocytes. As shown in **FIG. 18**, an anti-Dectin-1 (2M24)/anti-hCD94 bispecific induced coupling of Dectin-1-expressing cells and CD94-expressing cells. Thus, bispecific antibodies that bind Dectin-1 can mediate coupling of Dectin-1-expressing cells with a variety of target cells.

Example 3: Generation of bispecific anti-Dectin-1 antibodies using streptavidin-biotin.

[0269] This example describes the biochemical and functional characterization of bispecific antibodies that bind Dectin-1 generated using streptavidin-biotin conjugation.

Materials and Methods

Generation of bispecifics

[0270] mSA was genetically fused to either Fab 2M24 or full length 2M24. Chimeric fusions were incubated with biotinylated target antibodies to generate a bispecific comprising a Dectin-1-binding arm and a second arm binding a target receptor or protein of interest.

Full-length 2M24 sequence fused to mSA:

QVQLVQSGAEVKKPGASVKVSCKSSGYTFTDYYIHWVRQAPGQGLEWMGWINPNSGDTNYAQ
KFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGQGTLVTVSSASTKGPSVF
PLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSS
LGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTC
VVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKV
SNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPEN
NYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGG
GSGGGSEFASAEAGITGTWYNQHGSTFTVTAGADGNLTGQYENRAQGTGCQNSPYTLTGRYNG
TKLEWRVEWNNSTENCHSRTEWRGQYQGGAEARINTQWNLTYEGGSGPATEQGQDTFTKVKPS
AASGS (SEQ ID NO:127)

Fab 2M24 sequence fused to mSA:

QVQLVQSGAEVKKPGASVKVSCKSSGYTFTDYYIHWVRQAPGQGLEWMGWINPNSGDTNYAQ
KFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGQGTLVTVSSASTKGPSVF
PLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSS
LGTKTYTCNVDHKPSNTKVDKRVGGGSGGGSGGGSEFASAEAGITGTWYNQHGSTFTVTAGAD

GNLTGQYENRAQGTGCQNSPYTLTGRYNGTKLEWRVEWNNSTENCHSRTEWRGQYQGGAEAR INTQWNLTYEGGSGPATEQGQDTFTKVKPSAASGSAAAGASHHHHHH (SEQ ID NO:128)

Antibody-dependent targeted phagocytosis of Phrodo-labeled beads

[0271] Antibody-dependent targeted phagocytosis of Phrodo-labeled beads was performed as described in Example 2. To monitor phagocytosis by flow cytometry, HEK cells overexpressing Dectin-1 were incubated with biotin beads conjugated to Fab 2M24-mSA for 30 minutes on ice or at 37 °C for 30 minutes, followed by washing with PBS twice. Phagocytosis was assessed by detecting activated Phrodo red within the HEK cell/beads duplet population by flow cytometry in the PE channel using a CytoFlex flow cytometer (Beckman Coulter, Atlanta, GA).

Results

[0272] To enable the efficient generation of bispecific antibodies, a novel strategy was developed which utilizes the high affinity interaction of streptavidin and biotin. A monomeric streptavidin (mSA) construct was fused to the Fc-domain of 2M24, or CH1 domain of Fab 2M24. The recombinant fusion proteins were incubated with various biotinylated antibodies of interest to assemble the bispecifics. A schematic of this strategy is shown in **FIGs. 19A-19B**.

[0273] This fusion technology enables the high-throughput generation and screening of bispecific antibodies. To test this approach, a Fab 2M24-mSA fusion protein was generated and purified. As shown in **FIGs. 20A-20C**, the Fab 2M24-mSA fusion showed high affinity binding (EC50 = 1.45 nM) to Dectin-1 expressing cells. This Fab 2M24-mSA fusion protein can be combined with various biotinylated antibodies against targets of interests. Moreover, the Fab 2M24-mSA fusion also induced binding and phagocytosis of beads by Dectin-1-expressing HEK 293 cells (**FIGs. 21A-21B**), indicating that the Fab version of the 2M24 antibody can efficiently promote phagocytosis in cells expressing Dectin-1.

[0274] Using the anti-Dectin-1-streptavidin fusion, bispecifics against various targets (e.g., CD20, CD19, CD70, amyloid B (1-42)) were developed. As shown in **FIGs. 22A-22D**, these bispecifics showed high homogeneity based on HPLC analysis. These data demonstrate robust feasibility of this technology for bispecific antibody generation.

[0275] Next, the anti-Dectin-1 bispecifics generated using the Fab 2M24-mSA fusion protein were evaluated for their ability to induce cell coupling. As shown in **FIG. 23**, the Fab 2M24-mSA/biotin anti-hCD20 bispecific induced coupling of Dectin-1-expressing HEK293 cells and CD20-expressing B cells (Raji cell line). This interaction can promote Dectin-1 clustering, which induces cytokine secretion by effector cells, triggers phagocytosis of target cells, and leads to neo-antigen presentation and activation of adaptive immune cells (B and T-cells).

Example 4: Targeted phagocytosis of amyloid deposits using anti-Dectin-1 bispecific antibodies

[0276] This example describes the use of bispecific antibodies that bind Dectin-1 in the targeted delivery of pathogen antigens to phagocytic cells.

[0277] Dectin-1-induced targeted phagocytosis can be used to mediate amyloid clearance by antigen presenting (e.g., monocytes, macrophages, dendritic cells, and neutrophils), and maximize depletion of circulating amyloid precursors (free light chains) and deposited amyloid fibrils. The targeted phagocytosis relies on the bispecific antibody targeting of Dectin-1 (by 2M24) and AL amyloids (by an amyloid-reactive antibody or serum amyloid protein P antibody).

[0278] To test this approach, recruitment or presence of antigen presenting cells to sites of amyloid deposits is first demonstrated. Immune cell populations in freshly isolated, amyloid-laden tissues from AL amyloidosis patients are phenotyped. Frequency of antigen presenting cells (*e.g.*, macrophages, monocytes, neutrophils, and dendritic cells) is determined. Dectin-1 expression on APCs in AL amyloidosis patient tissues is assessed.

[0279] Then, bispecific antibodies comprising a Dectin-1 binding arm (*e.g.*, clone 2M24) and amyloid-binding arm (based on external antibodies) are developed. For proof-of-concept studies, phagocytosis of AL amyloid fibrils by circulating monocytes, monocyte-derived macrophages (*in vitro* differentiated) or patient-derived macrophages (*in situ*) is demonstrated with Dectin-1 bispecific antibodies prepared with external antibodies (**FIG. 24**). An antibody discovery campaign to identify high affinity binders to amyloid fibrils or amyloid precursors is initiated, from which the resulting antibodies are used to further develop Dectin-1 bispecific antibodies to target amyloid deposits.

Example 5: Targeted phagocytosis of mast cells using anti-Dectin-1 bispecific antibodies

[0280] This example describes the use of bispecific antibodies that bind Dectin-1 in the targeted delivery of pathogen antigens to phagocytic cells.

Materials and Methods

Bead phagocytosis assay

[0281] Large (~ 16.5 μm) polystyrene anti-mouse Fc IgG beads were labeled with a pH-sensitive fluorescent dye (pHrodo red) and conjugated with an anti-Dectin-1 antibody or isotype control. For the phagocytosis assay, the beads were incubated with cultured dendritic cells at a ratio of 1:3 (cells: beads). Bead phagocytosis was monitored by IncuCyte live cell imaging. Phagocytosis was quantified using the IncuCyte analysis software and expressed as total integrated intensity (total sum fluorescent intensity) of red objects (pHrodo fluorescense) in the image.

[0282] Mastocytosis is characterized by a pathological accumulation of mast cells in one or more organs. Given the tissue-resident nature of mast cells, and difficulty in accessing these cells therapeutically, tissue-resident macrophages can be engaged and enlisted to deplete and reduce

pathological levels of mast cells. As described in Example 1, engagement of Dectin-1 can promote phagocytosis of particles with similar size to cells, including mast cells. Thus, for the targeted depletion of mast cells, the Dectin-1 induced targeted phagocytosis platform can be applied.

[0283] First, bispecific antibodies with a macrophage-targeting arm (via Dectin-1 binding) and a mast cell-targeting arm (via mast cell surface antigen) are developed, as depicted in **FIG. 25A**. Potential mast cell surface antigens/receptors that can be used as lead candidates for bispecific development are summarized in **FIG. 25B**. These bispecific antibodies are then evaluated for their ability to bind and target mast cells for phagocytosis by Dectin-1 expressing cells and deplete patient mast cells *in situ*. Phagocytosis of in vitro-differentiated mast cells or mast cell lines by monocyte-derived macrophages (in vitro differentiated) or patient-derived macrophages (in situ) is demonstrated using Dectin-1 bispecific antibodies.

[0284] The presence or recruitment of antigen presenting cells (*e.g.*, macrophages, monocytes, neutrophils, and dendritic cells) is demonstrated in patient tissues/organs with high number of mast cells. Immune cell populations are phenotyped in fresh tissues isolated from mastocytosis patients. Dectin-1 expression is assessed on APCs. Binding of external antibodies is assessed on donor mast cells.

[0285] Given the large size of mast cells, we assessed if Dectin-1 can promote phagocytosis of large entities by conjugating anti-Dectin-1 antibody to large beads (~16.5um), which are similar in size to large cells. Since macrophages are large phagocytic cells and can ingest large targets, the phagocytosis assay for large beads was performed using macrophages differentiated from monocytes in the presence of MCSF for 6 days. As shown in **FIG. 26**, anti-Dectin-1 antibody promoted the directed phagocytosis of large beads in cultured human macrophages. Anti-Dectin-1-conjugated beads were more readily engulfed by the macrophages compared to isotype control-conjugated beads. These data support that targeting Dectin-1 enables targeting of large cells, such as mast cells (size: 16-20μm), for phagocytosis.

Example 6: Targeted depletion of microbes using anti-Dectin-1 bispecific antibodies

[0286] This example describes the use of bispecific antibodies that bind Dectin-1 in the targeted phagocytosis of microbes.

Materials and Methods

Binding to H3N2 flu virus by ELISA

[0287] To assess the binding of the anti-Dectin-1/a-hemagglutinin bispecific antibody to the H3N2 flu virus, H3N2 flu particles at 2.5, 5, and 10ug/mL were coated overnight on high binding 96-well plates. The plates were washed twice with PBS, blocked with 3% BSA in PBS/Tween-20 0.05% for 1 hour at RT, followed by more washes with PBS/Tween-20 0.05%. Primary antibodies, including anti-Dectin-1 (15E2), anti-hemagglutinin (12CA5), anti-Dectin-1/anti-hemagglutinin bispecific, and isotype controls were incubated at 20nM for 1 hour at RT. The plates were then washed with PBS/Tween-20 0.05% twice, and a secondary anti-mouse Fcg: HRP at 1:5000 was incubated for 1 hour at RT. Finally, the plates were

washed, incubated with TMB substrate for 30 minutes, and the reaction was stopped with 2N H_2SO_4. The plates were read at 450nm on a plate reader.

[0288] Innate immune cells play a vital role in recognition and elimination of microbial pathogens. To aid phagocytes in attacking bacteria, viruses, or fungal pathogens, a bispecific comprising a Dectin-1-targeting arm which binds antigen presenting cells (macrophages, monocytes, dendritic cells, and neutrophils) and a second arm targeting an antigen expressed on the surface of pathogens can be used for Dectin-1-induced targeted depletion **(FIG. 27).** The targeted phagocytosis of pathogens enables effector cells to efficiently recognize a target pathogen and secrete cytokines and proteases that can directly kill the bound pathogen Furthermore, the bispecific antibody can mediate Dectin-1 clustering, induced targeted-phagocytosis of the bound target. Finally, following degradation of the target, target antigens are presented and modulates the adaptive immune response which further enables the host organism to fight off the pathogen.

[0289] As a proof-of-principle, high affinity antibodies against pathogen-specific surface antigens of interest are identified and used to generate bispecific antibodies comprising a Dectin-1-binding arm (anti-Dectin-1 antibody 2M24) and a pathogen-targeting arm. The anti-Dectin-1/anti-pathogen bispecific antibodies are tested for target binding, cytokine secretion by phagocytes following target engagement, target phagocytosis and degradation of the pathogen, and target antigen presentation. Moreover, high affinity antibodies are developed to validate the pathogen targets and are used to subsequently develop Dectin-1 bispecific antibodies from lead candidates.

[0290] To test for the targeted delivery of pathogen to phagocytic cells antigens, a bispecific antibody with a Dectin-1-binding arm and a second arm that binds Hematogglutinin from influenza H3N2 virus was generated. The anti-Dectin-1/anti-Hemagglutinin bispecific antibody was then tested for binding using both ELISA and flow cytometry. As shown in **FIGs. 28A-28B**, the anti-Dectin-1/anti-Hemagglutinin bispecific antibody bound efficiently to both the H3N2 flu virus and to HEK cells expressing Dectin-1. This antibody format could be used to target the flu virus or an antigen of the flu virus to antigen presenting cells (*e.g.,* dendritic cells, macrophages).

Example 7: Targeted delivery of antigens for vaccine development

[0291] This example describes the targeted delivery of viral antigens to phagocytic cells.

Materials and Methods

Bead phagocytosis assay

[0292] Small (~ 3.4 μm) polystyrene anti-mouse Fc IgG beads were labeled with a pH-sensitive fluorescent dye (pHrodo red) and conjugated with an anti-Dectin-1 antibody or isotype control. For the phagocytosis assay, the beads were incubated with cultured dendritic cells at a ratio of 1:3 (cells: beads). Bead phagocytosis was monitored by IncuCyte live cell imaging. Phagocytosis was quantified using the

IncuCyte analysis software and expressed as total integrated intensity (total sum fluorescent intensity) of red objects (pHrodo fluorescense) in the image.

Labelling of polysterene beads with pHrodo and conjugation to antibodies

[0293] Labelling of polysterene beads with pHrodo and conjugation to antibodies was performed as described earlier.

[0294] To coat polystyrene beads with the SARS-Cov-2 spike protein S1, goat anti Rabbit IgG (Fc) beads (Spherotech) were labeled with pHrodo Red and conjugated to a rabbit anti-Flag antibody (Cell Signaling) as described above. Flag-tagged Spike protein (Genscript) was then coupled to pHrodo/anti-Flag beads, and unbound Spike protein was washed off with PBS.

Antibody-dependent targeted phagocytosis of Phrodo labeled beads

[0295] For phagocytosis of SARS-CoV-2 spike protein coated beads, the beads were pre-incubated with anti-Dectin-1/anti-SARS-CoV-2 spike protein bispecific (anti-SARS-CoV-2 spike protein antibody was purchase from Genscript) for 60 minutes in RT and unbound antibody was washed off. The beads were then mixed with HEK cells.

Results

[0296] Dendritic cells are specialized antigen-presenting cells. Targeting an antigen expressed on a disease-causing agent (cancer cell, pathogen, or protein-aggregate) or the agent itself to dendritic cells through Dectin-1 can potentially elicit a protective immune response directed against the antigen and the disease-causing agent from which it was derived. This response will involve T cell activation and expansion, cytokine secretion and B cell activation. Thus, a Dectin-1 antibody-targeted vaccine could be designed to deliver antigens to dendritic cells and promote the recognition and elimination the disease-causing agent (e.g., cancer cells or pathogen). Target antigen could be fused to an anti-Dectin-1 antibody for delivery to APCs (**FIG. 29A**), or anti-Dectin-1 bispecific antibody could be used to target delivery of a disease-causing agent to APCs (**FIG. 29B**).

[0297] To determine if phagocytosis in human dendritic cells can be promoted by antibody engagement of Dectin-1, purified monocytes (CD14+) from human PBMC were differentiated to Dendritic cells in the presence of IL4/GMCSF. After 6 days the dendritic cells were incubated with pHrodo-labeled polystyrene beads conjugated with the 15E2 anti-Dectin-1 antibody or an isotype control. As shown in **FIG. 30**, anti-Dectin-1 antibodies promoted directed phagocytosis of beads in cultured monocyte-derived dendritic cells. Significantly more phagocytosis of anti-Dectin-1-conjugated beads than of isotype-conjugated beads was observed, as evidenced by the bright red phrodo particles within the cells. Dendritic cells are specialized antigen-presenting cells. Targeting an antigen on a disease-causing agent (*e.g.*, a cancer cell, pathogen, or protein aggregate), or the agent itself, to dendritic cells through Dectin-1 can potentially elicit a protective immune response directed against the antigen and the disease-causing agent from which

it was derived. This response can involve T cell activation and expansion, cytokine secretion, and B cell activation. Therefore, a Dectin-1 antibody-targeted vaccine can be designed to deliver antigens to dendritic cells and promote the recognition and elimination of a disease-causing agent (*e.g.*, a cancer cell or pathogen).

[0298] Targeting of a different virus, SARS-CoV-2, using Dectin-1 agonist bispecific antibodies was also evaluated. A bispecific antibody was generated using click chemistry to target Dectin-1 and the spike S1 protein of SARS-CoV-2. The spike protein was coated onto beads, and the beads were then engulfed in the presence of the anti-Dectin-1/anti-SARC-CoV-2 spike S1 bispecific (**FIG. 31A**). The anti-Dectin-1/anti-SARS-CoV-2 spike S1 bispecific induced coupling between Dectin-1 expressing HEK 293 cells and the spike coated beads (**FIG. 31B**), as well as promoted phagocytosis of the spike-coated beads by the Dectin-1-expressing cells (**FIG. 31C**). Based on these results, the anti-Dectin-1/anti-SARS-CoV-2 spike S1 bispecific could mediate targeted delivery of SARS-CoV-2 Spike protein to macrophages.

Conclusions

[0299] Bispecific antibody comprising a Dectin-1-binding arm and a second arm that binds an antigen from a pathogen, such as influenza virus or SARS-CoV-2 as described in this example, can promote engulfment of the target pathogen, and presentation of the antigens followed by activation and expansion of T cells and antibody production by B cells. The adaptive immune response can promote elimination of the virus and virus-infected cells. Dectin-1 antibody-targeted vaccine approach has the potential to work against other pathogens of bacterial or viral origin.

[0300] Various anti-Dectin-1 (*e.g.*, 2M24)/antigen-specific bispecific antibodies are developed and demonstrated to efficiently bind to APCs. Internalization of the targeted antigen from APCs is assessed. Methods to assess antigen presentation of the targeted antigen on the surface of dendritic cells are developed. Activation of CD4+ and CD8+ T cells (T cell expansion and cytokine secretion) is assessed from dendritic cells that have received antigen through Dectin-1. B cell activation and antibody production against the antigen are assessed. Mice are vaccinated, and adaptive immune response is assessed in vivo, along with protection against the disease caused by the pathogen/malignant cells.

Example 8: Bispecific design for development of a human bispecific antibody targeting Dectin-1 and a disease target or antigen

[0301] To enable the assembly and efficient production of highly purified and active bispecifics, design principles were adopted based on previously reported strategies including "knobs-into-holes" (Ridgway, 1996; patent US8679785B2), DuetMab (Mazor, 2015; patent EP3452089A2), single-step Protein A and G avidity purification methods (Ollier, 2019; AU2018204314B2), and mutations to eliminate FcR binding (patent WO 2016/081746 A2). Assembly of complete bispecific involves expression of 4 individual

subunits, *e.g.*, cloned into expression vectors such as pFUSE. A diagram of an exemplary anti-Dectin-1 bispecific antibody is shown in **FIG. 32A**.

[0302] As shown in Table 1, bispecific antibodies using this design were constructed for proof-of-concept studies. These bispecific antibodies have one arm that targets hDectin-1 and a second arm that targets hCD20, hHER2, hCD70, or a protein on RSV. The bispecific antibodies described in Table 1 were generated by expressing all 4 chains and purifying to 95% purity and homogeneity. All bispecifics were found to bind their respective targets.

Table 1. Bispecific antibodies targeting human Dectin-1 and antigen expressed on cancer cells/disease targets.

Name	Target 1	Target 2
2M24/CD20 hIgG1 (fucosylated or afucosylated)	hDectin-1 (variable domain from clone 2M24)	hCD20 (variable domain based on Rituximab antibody)
2M24/HER2 hIgG1 (fucosylated or afucosylated)	hDectin-1 (variable domain from clone 2M24)	hHER2 (variable domain based on Trastuzumab antibody)
2M24/CD70 hIgG1 (fucosylated or afucosylated)	hDectin-1 (variable domain from clone 2M24)	hCD70 (variable domain based on Cusatuzumab antibody)
2M24/RSV hIgG1 (fucosylated or afucosylated)	hDectin-1 (variable domain from clone 2M24)	This bispecific is used as an isotype control antibody for POC studies. The second arm binds a protein on respiratory syncytial virus (RSV).

[0303] Variable domains for the antibody arm opposite anti-Dectin-1 in Table 1 were as follows.

CD20 VH:

QVQLQQPGAELVKPGASVKMSCKASGYTFTSYNMHWVKQTPGRGLEWIGAIYPGNGDTSYNQKFKGKATLTADKSSSTAYMQLSSLTSEDSAVYYCARSTYYGGDWYFNVWGAGTTVTVSA (SEQ ID NO:129)

CD20 VL:

QIVLSQSPAILSASPGEKVTMTCRASSSVSYIHWFQQKPGSSPKPWIYATSNLASGVPVRFSGSGSGTSYSLTISRVEAEDAATYYCQQWTSNPPTFGGGTKLEIK (SEQ ID NO:130)

HER2 VH:
EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPTNGYTRYADSV KGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYWGQGTLVTVSS (SEQ ID NO:131)
HER2 VL:
DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLYSGVPSRFSGS RSGTDFTLTISSLQPEDFATYYCQQHYTTPPTFGQGTKVEIK (SEQ ID NO:132)
CD70 VH:
EVQLVESGGGLVQPGGSLRLSCAASGFTFSVYYMNWVRQAPGKGLEWVSDINNEGGTTYYADS VKGRFTISRDNSKNSLYLQMNSLRAEDTAVYYCARDAGYSNHVPIFDSWGQGTLVTVSS (SEQ ID NO:133)
CD70 VL:
QAVVTQEPSLTVSPGGTVTLTCGLKSGSVTSDNFPTWYQQTPGQAPRLLIYNTNTRHSGVPDRFS GSILGNKAALTITGAQADDEAEYFCALFISNPSVEFGGGTQLTVL (SEQ ID NO:134)
RSV VH:
QVTLRESGPALVKPTQTLTLTCTFSGFSLSTSGMSVGWIRQPPGKALEWLADIWWDDKKDYNPS LKSRLTISKDTSANQVVLKVTNMDPADTATYYCARSMITNWYFDVWGAGTTVTVSS (SEQ ID NO:135)
RSV VL:
DIQMTQSPSTLSASVGDRVTITCKCQLSVGYMHWYQQKPGKAPKLLIYDTSKLASGVPSRFSGSG SGTAFTLTISSLQPDDFATYYCFQGSGYPFTFGGGTKLEIK (SEQ ID NO:136).

[0304] These hDectin-1 bispecific antibodies engage 3 targets: Dectin-1 on myeloid cells, an antigen on a target cell or disease-causing agent, and Fc receptors on myeloid and NK cells, eliciting robust immune stimulation and phagocytosis (**FIG. 32B**). In particular, bispecific antibodies with a non-fucoyslated, active hIgG1 Fc domain allow the bispecific antibody to recruit myeloid cells (*e.g.*, monocytes, macrophages, and dendritic cells) and natural killer (NK) cells to eliminate disease-causing target cells, such as tumor cells expressing specific antigens. In the context of cancer, and without wishing to be bound to theory, dual engagement of Dectin-1 and Fcγ receptors on myeloid and NK cells is thought to elicit a strong immune response that ultimately eliminates cancer cells via the following actions: (1) bispecific antibody-induced cross-linking of Dectin-1 and Fcγ receptors leads to ITAM-dependent activation of downstream inflammatory pathways and release of immuno-modulatory cytokines and cytotoxic proteins (proteases, perforin) which modulates the tumor microenvironment and may directly kill targeted cells; (2) bispecific antibody-induced clustering of Dectin-1 and Fcγ receptors triggers phagocytosis and elimination of targeted cancer cells by monocytes, macrophages and dendritic cells; and (3) phagocytosed antigens are presented by macrophages and DCs, a process that triggers a T cell immune response aimed at eliminating cancer cells.

[0305] The 2M24/CD20 and 2M24/RSV bispecific antibodies described in Table 1 were tested for binding to cells expressing human Dectin-1 or CD20. 2M24/RSV was used in all assays as an isotype control for the target binding arm. The bispecific variants tested here contained mutations in the hIgG1 Fc domain (hIgG1 inert) that eliminate Fc binding to Fc receptors (L234A, L235E, and G237A, according to EU numbering). Binding of 2M24/CD20 or 2M24/RSV bispecific to HEK293 cells stably expressing human Dectin-1 was assessed by flow cytometry (**FIG. 33A**). 2M24/CD20 and 2M24/RSV hIgG1 inert bispecific antibodies were able to bind cells expressing human Dectin-1 with similar affinities (cell-based binding EC50 values of 1.4 and 1.7 nM, respectively). Thus, 2M24/CD20 or 2M24/RSV bispecific antibodies displayed high affinity binding to Dectin-1-expressing HEK293 cells.

[0306] Binding of Rituximab, 2M24/CD20, or 2M24/RSV hIgG1 active or inert bispecific antibodies was also assessed using the CD20-expressing B cell lymphoma Raji cell line (**FIG. 33B**). 2M24/CD20 bispecific (active or inert hIgG1 isotypes) antibodies were able to bind to CD20-expressing Raji cells, but with at least 10-fold reduced affinity compared to Rituximab. Without wishing to be bound to theory, it is thought that the difference in CD20 binding affinity between 2M24/CD20 bispecific and Rituximab is likely mediated by the loss of avidity (monovalent versus bivalent binding) in the bispecific antibody.

[0307] Next, the ability of 2M24/CD20 bispecific antibody to induce coupling of cells expressing hDectin-1 and cells expressing hCD20 was assayed. Dectin-1-expressing HEK293 cells (effector) and CD20-expressing Raji cells (target) were differentially labeled with calcein green (effector) or calcein red (target) dyes. Labeled cells were co-cultured and treated with hIgG1 inert 2M24/CD20 or 2M24/RSV (control) bispecific antibody to induce effector: target coupling. Successful coupling of effector: target cells was indicated by the double-positive staining (Calcein green+, calcein red+, square box; **FIG. 34A**). Coupling efficiency (quantified as the percentage of total target cells that binds or couples to effector cells) was assayed using dose titration of bispecific antibody in co-cultures of effector: target cells (**FIG. 34B**).

[0308] These results indicate that 2M24/CD20 bispecific antibody can couple Dectin-1-expressing 'effector' cells and CD20-expressing 'target' cells with a potent EC50 of 0.17 nM. Despite the low affinity binding of 2M24/CD20 bispecific to CD20 on Raji cells (**FIG. 33B**), the 2M24/CD20 was highly efficient at coupling. These findings suggest that 2M24/CD20 binding affinity is enhanced by the high expression of Dectin-1 or CD20 on both effector and target cells (avidity), thereby promoting efficient coupling of the two cells. Based on these findings, it is thought that 2M24/CD20 bispecific antibody could effectively engage Dectin-1-expressing monocytes, macrophages or dendritic cells with target disease cells, such as B cell lymphoma, which express high levels of CD20. Effector: target engagement is the first step in the MOA of 2M24 bispecific antibodies.

[0309] Human IgG1 active isotype binds Fcγ receptors on NK cells or monocytes. Therefore, it was assessed whether the hIgG1 active isotype of 2M24/CD20 can trigger monocyte killing by NK cells (via antibody dependent-cellular cytotoxicity, ADCC) or other monocytes (Fratricide or antibody-dependent

cellular phagocytosis, ADCP). In this scenario, the active hIgG1 domain of 2M24/CD20 engages the Fcγ receptors on NK cells or monocytes, and Dectin-1 receptor on monocytes, thereby inducing Fcγ-mediated activation and depletion of target. PBMCs from two healthy donors – donor 76 (**FIG. 35A**) and donor 77 (**FIG. 35B**) were treated with increasing concentrations of 2M24/CD20 bispecifics (hIgG1 active or inert isotypes) and rituximab for 24 h, and subsequently analyzed by flow cytometry to quantify the levels of live, CD14+ monocytes remaining (as a % of isotype controls). No decrease in the number of monocytes was found in either donor, indicating that 2M24/CD20 active IgG1 did not induce monocyte depletion. Without wishing to be bound to theory, it is thought that 2M24/CD20 hIgG1 (active isotype) should not affect the levels of monocytes and thus poses minimal risk of infection.

[0310] Based on the proposed MOA of 2M24/CD20 bispecific antibody (described in **FIG. 32B**), B cell depletion by 2M24/CD20 hIgG1 (active isotype) bispecific antibody or Rituximab was assessed in order to compare B cell depletion. PBMCs from two healthy donors – donors 83 (**FIG. 36A**) and 84 (**FIG. 36B**) – were treated with increasing concentrations of the indicated antibodies for 24 hours, and subsequently analyzed by flow cytometry to quantify the levels of remaining live, CD19+ B cells (reported as a % of B cells in isotype control-treated PBMCs). Thus, in two healthy donors, high concentrations of 2M24/CD20 bispecific antibody induced superior B cell depletion (~80% reduction) compared to Rituximab (~40% reduction), despite the bivalent binding nature of Rituximab and ~10-fold difference in binding affinity (as shown in **FIG. 33B**). The unique mechanism of action of 2M24/CD20 active IgG1, which involves binding to Dectin-1 on myeloid cells, Fcγ receptors on NK cells and monocytes, and CD20 on target B cells (**FIG. 32B**), leads to an overall superior depletion of B cells compared to Rituximab. These data support the concept that Dectin-1 induced immune stimulation via 2M24/CD20 bispecific enhances depletion of the target cells.

[0311] Ability of 2M24/CD20 hIgG1 (active isotype) bispecific antibody or Rituximab (hIgG1) to downregulate CD19 expression on B cells in a process known as shaving or trogocytosis was assessed. Expression of CD19+ on B cells from two healthy donors – donor 83 (**FIG. 37A**) and donor 84 (**FIG. 37B**) – was quantified by flow cytometry following a 24-hour incubation with increasing concentration of 2M24/CD20 hIgG1 (active isotype) bispecific antibody, Rituximab, or isotype controls. The mean fluorescent intensity (MFI) for CD19 staining using anti-CD19 (BV605 conjugated) was used to evaluate the effect of 2M24/CD20 bispecific and Rituximab on CD19 expression on B cells. In PBMCs from donor 83, the EC50 with respect to CD19 expression was 0.014nM for rituximab and 0.080nM for 2M24/CD20 hIgG1 bispecific (**FIG. 37A**). In PBMCs from donor 84, the EC50 with respect to CD19 expression was 0.013nM for rituximab and 0.090nM for 2M24/CD20 hIgG1 bispecific (**FIG. 37B**). Both 2M24/CD20 active IgG1 bispecific Ab and Rituximab led to downregulation of CD19 expression on B cells. Interestingly, Rituximab demonstrated at least five-fold more potent shaving compared to 2M24/CD20 bispecific Ab. Downregulation of target CD20 on B cells was previously reported as a mechanism by which malignant B cells escape Rituximab-mediated depletion (Beum, P.V. *et al.* (2006) *J.*

Immunol. 176:2600-2609). These findings therefore suggest that 2M24/CD20 active IgG1 bispecific may be superior in depleting B-cells as compared to Rituximab due to reduced shaving potential.

[0312] Immune stimulation triggered by 2M24/CD20 active IgG1 bispecific antibody led to secretion of a unique repertoire of cytokines compared to Rituximab (**FIG. 38**). ELISA-based (mesoscale discovery) quantification of cytokines was undertaken in supernatants isolated from healthy donor PBMCs treated with 2M24/CD20 active hIgG1 bispecific, Rituximab, or isotype controls. PBMCs were stimulated with antibodies overnight, and supernatants were subsequently analyzed by MSD. Cytokines tested were IFNγ, IL-12p70, IL-6, TNFα, IL-1β, IL-4, IL-13, IL-10, and IL-8. The results indicated that 2M24/CD20 active IgG1 triggered higher level and distinct cytokine activation in PBMCs compared to Rituximab. Furthermore, engagement of Dectin-1 and Fc receptor alone by the 2M24/RSV bispecific does not induce cytokine release, excluding the possibility of systemic cytokine activation. These findings highlight a unique MOA that distinguishes 2M24/CD20 active IgG1 bispecific antibody from Rituximab. Without wishing to be bound to theory, these findings further indicate that 2M24/CD20 could trigger release of Th1 and Th2-type of responses and promote immune stimulation of tumor microenvironment.

[0313] 2M24/CD20 hIgG1 (active isotype) bispecific antibody was also found to induce superior B-cell depletion and lower CD19 shaving compared to Rituximab in co-cultures of human macrophages and GFP-expressing Raji B cells. Co-cultures of human macrophages and Raji-GFP cells (3:1 ratio) were analyzed by flow cytometry in the presence of 2M24/CD20 hIgG1 (active isotype) bispecific, 2M24/RSV control, fucosylated Rituximab or isotype hIgG1 control (**FIG. 39A**). Co-cultures were incubated at 37°C for 24 hours and then stained with a PE a-CD206 Ab to label macrophages and a BV-605 a-CD19 antibody to label Raji cells. The number of the remaining live/Raji-GFP+ cells was assessed in the end of the experiment. The primary antibodies were used in a serial dose titration. CD19 was assessed on Raji-GFP cells after 24 hours (**FIG. 39B**), with B-cell receptor shown as the reduction in the CD19 MFI in the presence of a-Dectin-1/a-hCD20 bispecific or Rituximab. The EC50 with respect to CD19 expression was 0.020nM for rituximab and 0.95nM for 2M24/CD20 hIgG1 bispecific. These results demonstrate enhanced B-cell depletion (Fcγ receptor mediated) by the 2M24/CD20 bispecific antibody compared to Rituximab. Rituximab reduced the B-cell receptor CD19 surface levels more potently than the a-Dectin-1/a-hCD20 bispecific antibody. Similarly, B-cell receptor shaving has been observed for CD20 by Rituximab, and the reduction of the CD20 limits the effectiveness of Rituximab to deplete B-cell. Without wishing to be bound to theory, it is thought that these data indicate that the superiority of the 2M24/CD20 hIgG1 (active isotype) bispecific to deplete B-cells is due to the lower B-cell receptor shaving compared to Rituximab. This highlights a differential mechanism of cell depletion by 2M24/CD20 hIgG1 (active isotype) bispecific.

[0314] B-cell depletion was also analyzed in single cell suspensions from kidney cancer tissue biopsies. Single cell suspensions from two Kidney cancer tissue biopsies were analyzed by flow cytometry in the presence of 2M24/CD20 hIgG1 (active or inert) bispecific antibody, 2M24/RSV hIgG1 controls, fucosylated Rituximab, and respective isotype controls. Kidney cancer tissue biopsies were dissociated to

single cell suspensions and treated with primary antibodies (2 μg/ml) for 24 hours at 37°C. Immune cell populations were analyzed by flow cytometry (**FIGS. 40A & 40B**). The number of the remaining live B cells was assessed by an anti-CD19 antibody and expressed as percentage of the CD45+ immune cell population (**FIG. 40C**). 2M24/CD20 active IgG1 bispecific antibody induced superior tissue B cell depletion as compared to Rituximab in single cell suspension of kidney cancer biopsies. The 2M24/CD20 hIgG1 (active isotype) bispecific antibody reduced B cells in the two kidney cancer donor biopsies by 44% and 46% (respectively), whereas Rituximab induced a B cell reduction of 33% and 18%, respectively (**FIG. 40C**). The data support the functionality of the 2M24/CD20 hIgG1 (active isotype) bispecific to deplete cells in cancer tissues via Dectin-1 induced immune stimulation and Fcγ receptor engagement. Without wishing to be bound to theory, it is thought that, since Dectin-1 is predominantly expressed on tumor associated macrophages (TAMs) in the above-described biopsies, 2M24/CD20 hIgG1 (active isotype) bispecific antibody may engage TAMs to enhance the target cell depletion.

[0315] Cytokine secretion by cultured macrophages and single cell suspension of kidney cancer biopsies stimulated with immobilized anti-Dectin-1 antibody (clone 2M24) or 2M24/CD20 bispecific antibody was tested. The anti-Dectin-1 antibody (clone 2M24), isotype control or the 2M24/CD20 bispecific antibody were immobilized overnight in U-bottomed polypropylene microtiter plates at 10 ug per well, followed by culture of human monocyte-derived macrophages (**FIGS. 41A & 41B**) or single cell suspension from kidney cancer biopsy (**FIG. 41C**). The cells were cultured for 24 hours and evaluation of TNFα secretion in the supernatant was assessed by ELISA. As a positive control, cells were stimulated with zymosan. Anti-Dectin 1 antibody (clone 2M24) was found to induce Dectin 1-clustering and TNFα secretion from human macrophages. These data provide evidence that the parental anti-Dectin-1 antibody (clone 2M24) can promote immune-stimulation in primary macrophage cultures as well as in single cell homogenate of cancer biopsies. Since Dectin-1 is expressed in myeloid cells, tumor associated macrophages in the cancer biopsies are expected to produce cytokines in response to the anti-Dectin-1 antibody stimulation. This promotes the transition of the tumor associated macrophages from anti-inflammatory to pro-inflammatory with strong anti-tumoral effects. Moreover, monovalent binding of the 2M24/CD20 bispecific antibody to Dectin-1 was sufficient to promote Dectin-1 clustering and immune-stimulation on macrophages.

[0316] Immune stimulation by immobilized anti-Dectin-1 antibody in single cell suspensions from kidney cancer biopsies were also analyzed (**FIG. 42**). Single-cell suspensions from kidney cancer biopsies were treated with immobilized anti-Dectin-1 antibody (clone 2M24) or isotype control hIgG4 antibody for 24 h. Supernatants were analyzed by ELISA for the release of various cytokines, including IFNγ, IL-6, TNFα, IL-23, IL-12p70, IL-10, and IL-13. These results show that activation of Dectin-1 on myeloid cells (in this example, Dectin-1 is expressed predominantly by tumor-associated macrophages, TAMs), elicited the release of specific repertoire of cytokines that are either directly downstream of Dectin-1 signaling pathway, or indirectly through activation of other immune cells. Without wishing to be bound to theory, it is thought that Dectin-1 engagement by 2M24 bispecific antibody promotes immune

stimulation that could modulate the tumor microenvironment to support the elimination of target-expressing cancer cells.

Example 9: Characterization of a bispecific antibody targeting Dectin-1 and CD20

[0317] This Example describes the further characterization of a bispecific antibody targeting human Dectin-1 and human CD20. The anti-Dectin-1 arm included the variable domains of 2M24, and the anti-CD20 arm included the variable domains of Rituximab (*see* SEQ ID Nos:129 and 130 for VH and VL domains, respectively).

Materials and Methods

CD16 expression on NK cells

[0318] Human PBMCs from a healthy donor were treated with a serial dilution of 2M24/CD20 hIgG1 KIF, Rituximab KIF, and isotype control RSV hIgG1 KIF antibodies. After 24 hours of treatment, PBMCs were stained with antibodies against lineage-specific markers for flow cytometry analysis. CD16 expression on CD56+ NK cells was quantified and compared to expression levels in the isotype control treated group.

CD19 expression on B cells

[0319] Human PBMCs from a healthy donor were treated with 0.1 nM of 2M24/CD20 hIgG1 KIF, Rituximab KIF, and isotype control RSV hIgG1 KIF antibodies. After 24 hours of treatment, PBMCs were stained with antibodies against lineage-specific markers for flow cytometry analysis. CD19 expression (MFI) on B cells was quantified.

B cell depletion in PBMCs

[0320] Human PBMCs from a healthy donor were treated with a serial dilution of the indicated antibodies. After 24 hours of treatment, PBMCs were stained with antibodies against lineage-specific markers for flow cytometry analysis. B cells were quantified relative to an untreated control group (indicated by the dotted line in **FIG. 45**).

B cell depletion in kidney cancer biopsies

[0321] Single-cell suspension was generated from kidney cancer biopsy and the cells were treated with 2M24/CD20 hIgG1, 2M24/RSV hIgG1, Rituximab hIgG1, and isotype control RSV hIgG1 antibodies. After 24 hours of treatment, the cells were stained with antibodies against lineage-specific markers for flow cytometry analysis. B cells were quantified as the percentage of CD19+ cells within the CD45+ immune cell population.

Results

[0322] First, the effect of the 2M24/CD20 bispecific on CD16 expression was examined in human NK cells. CD16 is required for ADCC activity by NK cells, therefore the loss of CD16 expression can decrease the cytotoxic potential of NK cells. Rituximab induced potent and robust shedding of CD16 on NK cells compared to 2M24/CD20 hIgG1 KIF (**FIG. 43**). In contrast, CD16 levels on NK cells were better maintained after 2M24/CD20 bispecific antibody treatment compared to rituximab treatment. Without wishing to be bound to theory, it is thought that 2M24/CD20 bispecific has the potential to better preserve NK cell cytotoxic potential.

[0323] Next, the effect of the 2M24/CD20 bispecific on CD19 expression was examined in human B cells. Preserving target antigen expression is critical for therapeutic activity of monoclonal antibodies. B cell antigens such as CD20, CD19, and BCMA are validated immuno-oncology targets. CD19 is known to be downregulated via shaving/shedding following binding of anti-CD19 antibodies. Using CD20-targeting antibodies, a bystander effect was observed where CD19 expression was reduced upon treatment with Rituximab, but not with the 2M24/CD20 hIgG1 KIF bispecific (**FIG. 44**). CD19 levels on B cells were better maintained by 2M24/CD20 bispecific antibody compared to rituximab. Without wishing to be bound to theory, it is thought that, therapeutically, 2M24/CD20 bispecific may exhibit prolonged activity due to minimal impact on target antigen expression.

[0324] To compare rituximab with the anti-CD20 antibody obinutuzumab, 2M24 bispecific antibodies against CD20 were generated using the variable domain sequences from either Rituximab or Obinutuzumab. Obinutuzumab variable domain sequences were as follows. VH: QVQLVQSGAEVKKPGSSVKVSCKASGYAFSYSWINWVRQAPGQGLEWMGRIFPGDGDTDYNG KFKGRVTITADKSTSTAYMELSSLRSEDTAVYYCARNVFDGYWLVYWGQGTLVTVSS (SEQ ID NO:137); VL: DIVMTQTPLSLPVTPGEPASISCRSSKSLLHSNGITYLYWYLQKPGQSPQLLIYQMSNLVSGVPDR FSGSGSGTDFTLKISRVEAEDVGVYYCAQNLELPYTFGGGTKVEIK (SEQ ID NO:138).

[0325] In an ADCC/ADCP assay, 2M24/CD20 (derived from Rituximab sequence) demonstrated almost complete depletion of B cells, superior to that of 2M24/CD20 (derived from obinutuzumab) or parental bivalent antibodies and isotype control (**FIG. 45**). These data support utilization of the rituximab sequence for 2M24/CD20 bispecific development

Example 10: Characterization of a bispecific antibody targeting Dectin-1 and CD20 in an exploratory study in non-human primates

[0326] This Example describes the results of an exploratory study on the safety and efficacy of the bispecific antibody targeting human Dectin-1 and human CD20 described in Example 9 in cynomolgus monkeys.

Materials and methods

[0327] Three groups of Cynomolgus monkeys (1 male and 1 female per group) were treated with a single dose (5 mg/kg) of test articles: A) 2M24/CD20 hIgG1 KIF, B) 2M24/CD20 hIgG1 inert, and C) Rituximab hIgG1 KIF. Blood was collected at the indicated time points. Abbreviations for test articles (2M24/CD20 KIF, 2M24/CD20 inert, RTX KIF).

[0328] B cell levels were assessed by flow cytometry. Depletion was quantified by the number of CD19+ B cells remaining in samples post-dose compared to the levels before test-articles were administered. Bone marrow and lymph node aspirates were collected at the indicated time points, and B cell levels were assessed by flow cytometry. Depletion was quantified by the number of CD19+ B cells remaining in samples post-dose (Day 7) compared to the levels before test-articles were administered (Day -7).

[0329] For PBMC assay, PBMCs from a healthy Cyno were treated with a serial dilution of 2M24/CD20 hIgG1 KIF, Rituximab KIF, and isotype control RSV hIgG1 KIF antibodies. After 24 hours of treatment, PBMCs were stained with antibodies against lineage-specific markers for flow cytometry analysis. B cell depletion was quantified relative to the isotype control group.

Results

[0330] This exploratory study was designed to examine the safety and efficacy of 2M24/CD20 bispecific antibody in non-human primates. The study design is shown in **FIG. 46**. Cynomolgus monkeys were divided into three treatment groups comprising 2 animals (1 male, 1 female) per group. Each group was administered a specific test article at a single dose of 5 mg/kg. The test articles included: 1) 2M24/CD20 hIgG1 KIF, 2) 2M24/CD20 hIgG1 inert, and 3) Rituximab hIgG1 KIF. Animals were monitored daily, and samples such as whole blood, bone marrow, lymph node, and colorectal tissues were collected as indicated. The study was planned for 8 weeks.

[0331] As shown in **FIG. 47** (upper), 2M24/CD20 hIgG1 KIF bispecific antibody depleted B cells *in vivo* in Cynomolgus monkeys. Nearly complete and sustained B cell depletion (~98%) was observed in both animals treated with a single dose (5 mg/kg) of 2M24/CD20 hIgG1 KIF. In the Rituximab group (**FIG. 48**), one animal showed complete depletion, whereas the second showed robust yet incomplete depletion (~87%). Partial B cell depletion was observed for one animal in the 2M24/CD20 hIgG1 inert group (**FIG. 47** lower), whereas the second animal showed no depletion at Day 7. 2M24/CD20 hIgG1 KIF bispecific antibody was well-tolerated in cynomolgus monkeys.

[0332] 2M24/CD20 hIgG1 KIF bispecific also depleted bone marrow (**FIG. 49A**) and lymph node (**FIG. 49B**) B cells *in vivo* in Cynomolgus monkey. A single dose (5 mg/kg) of 2M24/CD20 hIgG1 KIF induced robust B cell depletion in the bone marrow (~87-88%) and partial depletion in the lymph node (60-78%) in both animals. In the Rituximab group, B cell depletion was also observed in both tissues. Partial B cell depletion was observed in the 2M24/CD20 hIgG1 inert group, except for animal CB764A with minimal B cell depletion in the lymph node.

[0333] 2M24/CD20 hIgG1 KIF bispecific antibody also induced robust depletion of Cyno B cells *ex vivo* (**FIG. 50**). 2M24/CD20 hIgG1 KIF induced robust depletion of B cells compared to Rituximab hIgG1 KIF. The maximum depletion achieved by Rituximab was ~30% of B cells, whereas 2M24/CD20 hIgG1 KIF bispecific demonstrated maximum depletion at ~50%.

Example 11: Purification and functional characterization of the 2M24/CD20 bispecific antibody in scFv format

[0334] This Example describes the production, purification, and characterization of a 2M24/CD20 bispecific antibody in which the Dectin-1 targeting arm (based on 2M24 variable domains) was an scFv fused to a human IgG1 Fc domain with knob-forming mutations, and the CD20 targeting arm was based on rituximab hIgG1 with hole-forming mutations. A diagram of the molecule is shown in **FIG. 51**. Knob-forming mutation on Dectin-1 targeting arm was T366W; hole-forming mutations on CD20 targeting arm were T366S, L368A, and Y407V. Without wishing to be bound to theory, it is thought that this format provides a universal platform for generating anti-Dectin-1 bispecific antibodies with simpler manufacturing requirements (*e.g.*, as compared to bispecific antibodies having an anti-Dectin-1 arm with multiple polypeptide chains).

[0335] 2M24 scFv/CD20 hIgG1 was expressed in Hek293 cells by transfecting 3 plasmids (2M24 scFv hIgG1 plasmid, CD20 heavy chain, and CD20 light chain). Supernatant was harvested after four days of expression and purified via Protein A. Aggregates were removed with size exclusion chromatography. As shown in **FIG. 52A**, the 2M24 scFv/CD20 hIgG1 bispecific antibody purified as a homogenous molecule on SEC.

[0336] Next, co-cultures of CD20-expressing Raji cells and the Dectin-1-expressing HEK reporter assay were treated with increasing concentration of 2M24 scFv/CD20 hIgG1 bispecific. Reporter activation was assessed by measuring SEAP levels (based on absorbance at 630 nm) in media. The bispecific molecule promoted targeted immune stimulation, as assessed by this NFkB reporter assay (**FIG. 52B**).

[0337] To examine B cell depletion, human PBMCs from a healthy donor were treated with a serial dilution of the indicated antibodies. After 24 hours of treatment, PBMCs were stained with antibodies against lineage-specific markers for flow cytometry analysis. B cells were quantified relative to an untreated control group (indicated by the dotted line in **FIG. 52C**). The results demonstrated that the 2M24 scFv/CD20 hIgG1 bispecific antibody, similar to the 2M24/CD20 hIgG1 KIF molecule, was able to deplete human B cells (**FIG. 52C**).

Example 12: Development and characterization of an anti-Dectin-1/anti-Trop-2 bispecific antibody

[0338] Trop-2 is a 323 aa type I membrane protein involved in calcium signal transduction, embryonic and fetal development, tight junction formation, and integrin-dependent signaling. Mutations in Trop-2 are associated with gelatinous drop-like corneal dystrophy, characterized by corneal amyloidosis and blindness. Trop-2 is overexpressed in various epithelial cancers, promoting cell proliferation, invasion

and neovascularization. High expression correlates with poor prognosis and survival in many cancers (notably in TNBC breast and NSCLC lung cancer). Sacituzumab govitecan (Trodelvy ®), a Trop-2–directed ADC, is the only therapeutic that is approved for the treatment of patients with metastatic TNBC. FDA-accelerated approval in 2020.

[0339] Therefore, Trop-2 is an oncology target that is clinically validated. However, there is an unmet need: Trodelvy® achieved a 33% response rate in a heavily pretreated population of patients with metastatic TNBC. Adverse reactions such as neutropenia, diarrhea, and vomiting are associated with Trodelvy toxin (SN-38) conjugate.

[0340] In contrast, an anti-Dectin-1-targeted approach has the potential to restrict anti-tumor activity to the disease microenvironment. Immune modulation and phagocytosis activities of 2M24 are tightly regulated by the presence of cancer cells. While Trodelvy® has a single mode of action (toxin conjugate delivery to induce target cell killing), the anti-Dectin-1-targeted approach utilizes multiple modes of action (targeted immune stimulation, phagocytosis, and antigen presentation) to eliminate cancer cells and promote lasting immunity.

[0341] This Example describes the development and characterization of an anti-Dectin-1 (2M24)/anti-Trop-2 bispecific antibody. Variable domains used for anti-Trop-2 were as follows. VH: QVQLQQSGSELKKPGASVKVSCKASGYTFTNYGMNWVKQAPGQGLKWMGWINTYTGEPTYTD DFKGRFAFSLDTSVSTAYLQISSLKADDTAVYFCARGGFGSSYWYFDVWGQGSLVTVSS (SEQ ID NO:139); VL: DIQLTQSPSSLSASVGDRVSITCKASQDVSIAVAWYQQKPGKAPKLLIYSASYRYTGVPDRFSGSG SGTDFTLTISSLQPEDFAVYYCQQHYITPLTFGAGTKVEIK (SEQ ID NO:140).

[0342] 2M24/Trop-2 bispecific antibody was purified by size exclusion chromatography, and purified antibody was analyzed by SDS-PAGE under non-reducing (NR) or reducing (R) conditions (**FIG. 53A**). 2M24/Trop2 bispecific antibody purified as a monodispersed molecule. 2M24/Trop2 bispecific antibody was found to bind with high affinity to Dectin-1-expressing HEK cells (**FIG. 53B**) and moderate affinity to Trop-2-expressing A431 cancer cell line (**FIG. 53C**).

[0343] To evaluate the level of Trop-2 expression on different cancer cells, cancer cell lines (A431 and SKBR3) were stained with anti-human PE Trop-2 or isotype control antibodies to evaluate Trop-2 expression. Receptor copy number was assessed by comparing the fluorescence intensity of fluorochrome-labeled microspheres with known amounts of the fluorophore to the fluorescence intensity of the labeled cells by flow cytometry. Trop-2 was found to be highly expressed on the cancer cell lines A431 and SKBR3, with receptor copy numbers of 8.4 million and 1.1 million, respectively (**FIG. 54**). These results demonstrate that Trop-2 polypeptide is highly expressed on cancer cells. High expression on cancer cells makes Trop-2 an attractive antigen for the targeted-killing of cancer cells by a 2M24/Trop-2 bispecific antibody.

[0344] Next, binding of the 2M24/Trop-2 bispecific antibody to Trop-2-expressing cell lines was examined. Cancer cell lines (HeLa, SiHa, BxPC-3, and Capan-2) were incubated with serial dilutions of

the 2M24/Trop-2 hIgG1bispecific antibody or an isotype control antibody as a single concentration (300 nM). The secondary antibody (AF647 goat Anti-Human) was used for detection by flow cytometry. Binding EC50 was determined using four-parameter logistic (4PL) non-linear regression. The results demonstrated that 2M24/Trop-2 bispecific antibody binds with variable sub-micromolar affinity to different Trop-2-expressing cell lines (**FIGS. 55A-55D**).

[0345] 2M24/Trop-2 bispecific antibody was assayed for ability to deplete Trop-2 expressing cell lines. Macrophages were generated by monocytes cultured with MCSF for 6 days. After differentiation, macrophages were co-cultured with Trop-2-expressing cancer cell lines, SKBR3 or A431, for 24 hours in the presence of 10 ug/ml 2M24/Trop-2 hIgG1 or 2M24/RSV hIgG1. To detect macrophages, PE-CD206 antibody was used. The cancer cells were detected either by pre-staining with Calcein AM (**FIG. 56A**, SKBR3 cells) or using an APC-EPCAM antibody (**FIG. 56B**, A431 cells). Phagocytosis was assessed by flow cytometry as double positive PE-CD206+Calcein+ cells in the single cell gate for SKBR3 cells (**FIG. 56A**) or remaining EPCAM+ cells for A431 cells (**FIG. 56B**). The results demonstrated that 2M24/Trop-2 bispecific antibody induced robust depletion of both cancer cell lines that express Trop-2. 2M24/Trop-2 bispecific antibody induced phagocytosis of Trop-2 expressing cell lines by macrophages. The cancer cell reduction was 56% for SKBR3 (**FIG. 56A**) and 87% for A431 cancer cells (**FIG. 56B**). The data provide strong evidence that the 2M24/Trop-2 bispecific antibody can direct the macrophages to eliminate cancer cells that express Trop-2.

[0346] Trop-2 expression in non-immune cells and Dectin-1 expression in tumor associated macrophages was assessed in a single-cell suspension of lung cancer biopsy tissue. Trop-2 was evaluated in CD45- cancer cells using a PE Trop-2 antibody. Expression of EPCAM was also confirmed in the same population. Expression of Dectin-1 was confirmed in tumor associated macrophages gated as CD45+CD11b+CD163+ cells after excluding B-cell, T-cells and NK-cells (**FIGS. 57A & 57B**). Dectin-1 is expressed in tumor associated macrophages and Trop-2 is expressed in cancer cells of lung cancer biopsy.

[0347] To examine whether 2M24/Trop-2 bispecific antibody was able to induce depletion of Trop-2-expressing cancer cells from lung cancer biopsy tissue, a single-cell suspension was generated from lung cancer biopsy, and the cells were treated with 2M24/Trop-2 hIgG1 or 2M24/RSV hIgG1 antibodies. After 24 hours of treatment, the cancer cells were quantified by staining with FITC CD45 and APC EPCAM antibodies for flow cytometry analysis. Cancer cell reduction was expressed as the percentage of CD45-EPCAM+ cells within the live cell population. The results demonstrated that 2M24/Trop-2 bispecific depleted Trop-2-expressing cancer cells in the lung cancer biopsy (**FIG. 58**). 2M24/Trop-2 bispecific antibody induced a 50% reduction of cancer cells expressing Trop-2 in the lung cancer biopsy. The data indicate that the 2M24/Trop-2 bispecific antibody can induce the phagocytosis and elimination of cancer cells by the tumor associated macrophages within the lung cancer tissue.

[0348] To assess Dectin-1 signaling as stimulated by 2M24/Trop-2 bispecific antibody, NFκB reporter HEK cells expressing Dectin-1 were incubated with A431 cancer cells in the presence of serial titration of

the 2M24/Trop-2 bispecific or 2M24/RSV antibodies. 2M24/Trop-2 bispecific engaged the two cell lines, promoting Dectin-1 receptor clustering and downstream activation of NFkB. Upon activation, SEAP is released into the media and used as a readout for Dectin-1activation. Media levels of SEAP were quantified using a spectrophotometer. 2M24/Trop-2 bispecific antibody induced robust stimulation of Dectin-1 and downstream NFκB activity (**FIG. 59**). These data indicate that the 2M24/Trop-2 bispecific promotes Dectin-1 signaling in effector cells in the presence of Trop-2 expressing cells. Therefore, the 2M24/Trop-2 bispecific antibody has the potential to drive Dectin-1 mediated immune stimulation by monocytes and macrophages that express high levels of Dectin-1.

[0349] Next, effects of 2M24/Trop-2 bispecific antibody on antigen presentation and T cell activation were examined. In this assay, as shown in **FIG. 59B**, monocyte-derived macrophages were co-cultured with SKBR3 breast cancer cells in the presence of 2M24/Trop-2 bispecific antibody. Macrophages are NY ESO-negative, while SKBR3 cells are NY ESO-positive. Bispecific antibody promoted phagocytosis and degradation of SKBR3 cells, and subsequent loading of the ESO peptide on MHC Class I or II on the surface of macrophages. Antigen-specific (ESO-reactive) T cells were then added to the co-culture assay where the TCR recognizes the ESO/MHC complex. This interaction triggered T cell activation, resulting in the release of cytokines (e.g., IFNγ) and expression of early activation markers such as CD69. This assay enables direct assessment of 2M24/Trop-2 bispecific-dependent phagocytosis and presentation of target cell antigens. The results are shown in **FIGS. 59C-59E**. Macrophages and SKBR3 breast cancer cells were co-incubated in the presence of 2M24/Trop-2 hIgG1 or control 2M24/RSV hIgG1 bispecific antibody. Phagocytosis or depletion of SKBR3 cells was assessed by flow cytometry by staining for EPCAM expression on SKBR3 cells (**FIG. 59C**). T cell activation is measured by the release of IFN gamma and expression of CD69. IFN gamma levels in the supernatants were quantified (**FIG. 59D**), and expression of CD69, an early activation marker, on T cells was assessed by flow cytometry (**FIG. 59E**). These data demonstrated that 2M24/Trop-2 bispecific antibody promotes antigen-presentation and T cell activation. The bispecific antibody 2M24/Trop-2 hIgG1 induced T cell activation by promoting phagocytosis of target cell or antigen by macrophages, and subsequent presentation of neoantigen (ESO-peptide) on MHC Class I on the surface of macrophages. These findings demonstrate that bispecific antibodies targeting Dectin-1 on antigen presenting cells (APCs) are sufficient to activate T cells.

Example 13: Development and characterization of an anti-Dectin-1/anti-Nectin-4 bispecific antibody

[0350] Nectin-4, or PVRL4, belongs to the nectin subfamily of immunoglobulin-like adhesion molecules that participate in Ca(2+)-independent cell-cell adhesion. It consists of three conserved immunoglobulin-like domains (V, C, C) in its extracellular region. Nectin-4 is mainly expressed during fetal development (embryo and placenta) and expression decreases with age.

[0351] Nectin-4 overexpression has been reported in many types of cancer. Its re-expression during tumor development makes it a tumor-associated antigen with the possibility of developing a targeted therapy. Silencing Nectin-4 inhibits tumor growth, cell proliferation and migration (Deng et al (2019)

Cancer Cell Int. 19:106; Nishiwada et al (2015) *J. Exp. Clin. Cancer Res.* 34:30). Nectin-4 interacts with ErbB2 and its trastuzumab-resistant splice variants, enhancing their activation and DNA synthesis. (Kedashiro et al (2019) *Sci. Rep.* 9:18997). Nectin-4 is cleaved by ADAM-17, and circulating Nectin-4 is detected in breast cancer (Fabre-Lafay et al. (2005) *J. Biol. Chem.* 280:19543-19550; Fabre-Lafay et al. (2007) *BMC Cancer* 7:73).

[0352] Enfortumab vedotin (ASG-22ME) is a first-in-class antibody-drug conjugate (ADC) directed against Nectin-4. Enfortumab vedotin monoclonal antibody binds to Nectin-4 expressing cells followed by the internalization and release of the anti-tumor agent monomethyl auristatin E (MMAE) into the cell, which result in cell cycle arrest and apoptosis. Enfortumab vedotin (Padcev) was approved for treatment of urothelial cancer in patients who have previously received PD-1 or PD-L1 inhibitor and a platinum-containing chemotherapy, based on NCT03219333 trial in Dec 2019.

[0353] In summary, Nectin-4 is a clinically validated target with an approved ADC. Nectin-4 is minimally expressed in normal tissues, but highly expressed in bladder, breast, cervical, pancreatic, lung, and esophageal cancers, among others. Nectin-4-positive solid tumor types have elevated levels of tumor-associated macrophages (TAMs). Dectin-1 expression on TAMs has been confirmed by single cell RNA sequencing and flow cytometry. As such, and without wishing to be bound to theory, it is thought that targeting Nectin-4 with a Dectin-1 bispecific antibody has the potential to treat Nectin-4-positive cancers by mechanisms including: (1) dual engagement of Nectin-4 on tumor cells and Dectin-1 on TAMs; (2) induction of phagocytosis and depletion of Nectin-4-expressing tumor cells by macrophages; (3) re-programming the immune-suppressive environment by inducing cytokine release through Dectin-1 clustering on TAMs; and/or (4) presenting tumor neoantigens, activating adaptive immune cells like T and B cells, and promoting durable anti-tumor immunity through engagement of professional antigen-presenting cells in the tumor microenvironment.

[0354] The bispecific 2M24/Nectin-4 antibody is shown in **FIG. 60A**, which uses the 2M24 anti-Dectin-1 variable domains and the Ha22 anti-Nectin-4 variable domains (VH: EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYNMNWVRQAPGKGLEWVSYISSSSSTIYYADSV KGRFTISRDNAKNSLSLQMNSLRDEDTAVYYCARAYYYGMDVWGQGTTVTVSS (SEQ ID NO:141); VL: DIQMTQSPSSVSASVGDRVTITCRASQGISGWLAWYQQKPGKAPKFLIYAASTLQSGVPSRFSGS GSGTDFTLTISSLQPEDFATYYCQQANSFPPTFGGGTKVEIK (SEQ ID NO:142)). DuetMab mutations on the heavy chain included F126C and C220V; mutations on the light chain included S121C and C214V. It was produced by transfecting 4 plasmids (2M24 heavy chain, 2M24 light chain, Nectin-4 heavy chain, and Nectin-4 light chain) into HEK293 cells. Supernatant was harvested after four days of expression and purified via Protein A (**FIG. 60B**).

[0355] Nectin-4 expression was assessed in cancer cell lines SKBR3 and A431 (**FIG. 61A**), and in single-cell suspension of prostate or ovarian cancer biopsies (**FIG. 61B**). Nectin-4 was detected using an anti-Nectin-4 mIgG2b antibody and an Alexa Fluor-647-conjugated secondary antibody. An isotype

mIgG2b antibody was used as a negative control for background staining. Nectin-4 expression was observed in cancer cell lines as well as cancer cells in the tumor biopsy tissues.

[0356] Binding of 2M24/Nectin-4 bispecific antibody to cells that express Dectin-1 or Nectin-4 was analyzed. Cell lines expressing Dectin-1 (HEK cells) or Nectin-4 (A431 cells) were incubated with serial dilutions of the 2M24/Nectin-4 hIgG1bispecific antibody or RSV hIgG1 (isotype control) to assess target binding. The secondary antibody (AF647 goat Anti-human IgG) was used for detection by flow cytometry. Binding EC50 values were determined using four parameter logistic (4PL) non-linear regression. The results demonstrated that 2M24/Nectin-4 bispecific antibody bound with high affinity to Dectin-1 and low affinity to Nectin-4 (**FIG. 62**).

[0357] Activity of the 2M24/Nectin-4 bispecific antibody was measured using an NFkB reporter assay. Schematic representation of assay setup is shown in **FIG. 63** (upper). NFkB reporter HEK cells expressing Dectin-1 were incubated with A431 cancer cells in the presence of serial titration of the 2M24/Nectin-4 bispecific or bivalent anti-Nectin-4 antibody. 2M24/Nectin-4 bispecific engages the two cell lines, promoting Dectin-1 receptor clustering and downstream activation of NFkB. Upon activation, SEAP was released into the media and used as a readout for Dectin-1activation. Media levels of SEAP were quantified using a spectrophotometer (**FIG. 63**, lower). The results demonstrated robust stimulation of Dectin-1 and downstream NFkB activity by the 2M24/Nectin-4 bispecific antibody.

[0358] 2M24/Nectin-4 bispecific antibody was analyzed for depletion of Nectin-4-expressing cancer cells. Macrophages were generated by monocytes cultured with MCSF for 6 days. After differentiation, macrophages were co-cultured with the Nectin-4-expressing cancer cell line A431 for 24 hours in the presence of 2M24/Nectin-4 bispecific, anti-Nectin-4 bivalent parental antibody, or RSV hIgG1 (isotype control). To detect macrophages (**FIG. 64A**), a PE-CD206 antibody was used. The cancer cells were detected using an APC-EPCAM antibody. Phagocytosis or depletion was assessed by quantifying the remaining EPCAM-positive cells. Data were reported as relative to the RSV control (**FIG. 64B**). 2M24/Nectin-4 bispecific antibody was able to deplete Nectin-4-expressing cancer cell lines via targeted phagocytosis by macrophages. Thus, this bispecific molecule has the potential for targeted depletion of Nectin-4-positive cancers.

Example 14: Development and characterization of an anti-Dectin-1 bispecific antibody targeting light chain amyloids

[0359] Light chain amyloidosis (AL) is caused by the expansion of an indolent B cell clone that produces an immunoglobulin light chain λ in 75–80% of cases and κ light chains in the remaining cases (Dispenzieri, A. and G. Merlini (2016). *Cancer Treat Res* 169: 273-318). High concentrations of misfolded light chain proteins are secreted into circulation and deposit in various organs. Amyloid deposition leads to irreversible organ failure and death if remains untreated. Greater than 4000 new AL cases are diagnosed annually in the U.S. 10-15% of multiple myeloma patients develop AL.

[0360] There is an unmet need for AL treatments. Myeloid cells such as tissue resident macrophages are involved in tissue amyloid clearance (Wall et al. (2012) *PLoS ONE* 7:e52686). Patients with hereditary transthyretin amyloidosis (ATTR) have impaired phagocytosis activity by myeloid cells (Suenaga et al. (2016) *PLoS ONE* 11:e0163944). Targeted phagocytosis of light chain amyloids via the Dectin-1 receptor on myeloid cells, like macrophages, monocytes and dendritic cells, is an attractive approach for amyloid clearance from tissues. The targeted myeloid engager bispecific strategy could enable Dectin-1 dependent, Fc-independent phagocytosis. Without wishing to be bound to theory, it is hypothesized that this approach may potentially overcome the limitations of current monoclonal antibody strategies that rely primarily on Fc-mediated signaling for amyloid clearance.

[0361] A bispecific antibody targeting Dectin-1 and light chain amyloids was constructed using the 2M24 anti-Dectin-1 and 11-1F4 anti-amyloid variable domains. 11-1F4 variable domains were as follows. VH: QVQLKESGPGLVAPSQSLSITCTVSGFSLSSYGVSWVRQPPGKGLEWLGVIWGDGSTNYKPNLM SRLSISKDISKSQVLFKLNSLQTDDTATYYCVTLDYWGQGTSVTVSS (SEQ ID NO:143); VL: DVVMTQTPLSLPVSLGDQASISCRSSQSLVHRNGNTYLHWYLQKPGQSPKLLIYKVSNRFSGVPD RFSGSGSGTDFTLKISRVEAEDLGLYFCFQTTYVPNTFGGGTKLEIK (SEQ ID NO:144).

[0362] The bispecific molecule was purified, and binding activity assayed. The parental bivalent antibody 11-1F4 hIgG1 (**FIG. 65A**, upper) and bispecific antibody 2M24/11-1F4 hIgG1 (**FIG. 65A**, lower) were purified in PBS by size exclusion chromatography. Purified antibodies were then evaluated for binding to recombinant light chain amyloids from different patients (AL30, AL47, AL48, and AL55) by Octet (**FIG. 65B** for 11-1F4 hIgG1 and **FIG. 65C** for 2M24/11-1F4 hIgG1). These results demonstrate that 2M24/11-1F4 bispecific antibody bound to light chain amyloids *in vitro*.

[0363] The ability of 2M24/11-1F4 bispecific antibody to induce phagocytosis of light chain amyloids was also examined. Monocytes were freshly isolated from healthy donor PBMCs and co-cultured with pHrodo-labeled light chain amyloids in the presence of either 2M24/11-1F4 hIgG1 inert bispecific antibody or the parental bivalent 11-1F4 hIgG1 antibody. Phagocytosis of light chain amyloids was monitored by the change in pHrodo fluorescence in the low-pH environment of phagosomes. Change in pHrodo activity over 24 hours was monitored in real-time using an Incucyte. The results demonstrated that 2M24/11-1F4 bispecific antibody induced robust phagocytosis of light chain amyloid fibrils compared to the control 11-1F4 hIgG1 antibody (**FIG. 66**). In this study, an Fc inactive or effectorless 2M24/11-1F4 demonstrated robust amyloid clearance activity, indicating that Dectin-1 binding was sufficient to promote phagocytosis. The 11-1F4 hIgG1 antibody contains an active Fc domain, however minimal clearance activity was observed. These findings suggest that targeting the phagocytic receptor Dectin-1 is an attractive approach treating light chain amyloidosis.

Example 15: Development and characterization of an anti-Dectin-1 bispecific antibody targeting amyloid beta in Alzheimer's disease (AD)

[0364] AD is the most common cause of dementia worldwide. It accounts for about 80% of all diagnosed cases (Weller and Budson, (2018) *F1000Res* 7). In the United States, AD claims more lives than prostate and breast cancer combined (Patterson, C. (2018). World Alzheimer Report 2018. The State of the Art of Dementia Research: New Frontiers. London, UK: Alzheimer's Disease International. Available at www.alz.co.uk/research/world-report-2018). AD is categorized into two forms: sporadic and familial. Ninety-nine percent of AD cases are sporadic, i.e., the exact cause of onset is unknown (Wang, J., Gu, B. J., Masters, C. L., and Wang, Y.-J. (2017). *Nat. Rev. Neurol.* 13, 612–623). Sporadic AD (SAD) or late-onset AD (LOAD) is most likely driven by genetic and environmental factors (Bondi, M. W., Edmonds, E. C., and Salmon, D. P. (2017). *J. Int. Neuropsychol. Soc.* 23, 818–831). The major genetic factor for SAD is the apolipoprotein E (APOE) gene. Other targets identified by GWAS studies include triggering receptor expressed in myeloid cells 2 (TREM2), complement C3b/C4b receptor 1 (CR1), CR1 (complement C3b/C4b receptor 1), CD33, and ABCA7 (Hansen, D. V., et al. (2018). *J Cell Biol* 217(2): 459-472). Many of these genes are expressed on microglial cells, suggesting a critical role of these cells AD etiology (Hansen, D. V., et al. (2018). *J Cell Biol* 217(2): 459-472). TREM2 is a microglial cell surface receptor central to phagocytosis, chemotaxis, survival, and proliferation of microglia (Carmona, S., Zahs, K., Wu, E., Dakin, K., Bras, J., and Guerreiro, R. (2018). *Lancet Neurol.* 17, 721–730). The TREM2 loss-of-function mutation R47H results in a two- to four-fold increase in the risk of AD like the risk associated with inheriting one copy of the e4 variant of APOE (Gratuze, M., Leyns, C. E. G., and Holtzman, D. M. (2018). *Mol. Neurodegener.* 13:66).

[0365] Most risk genes for Alzheimer's are highly expressed by microglia, suggesting that microglial dysfunction is associated with AD development and progression (Hansen, 2018). For instance, loss-of-function variants of the microglial phagocytic receptor TREM2 impairs clearance of amyloid β deposits and is linked to enhanced risk of dementia. The Dectin-1 phagocytic receptor is expressed on microglial cells and is not known to be a risk gene for AD. Therefore, without wishing to be bound to theory, it is thought that targeting Dectin-1 on microglial cells could induce targeted phagocytosis and clearance of amyloid beta in AD patients. Targeting Dectin-1 may bypass loss-of-function variants of microglial genes such as TREM2. Unlike current monoclonal antibody approaches such as aducanumab that rely on Fc receptors on microglial cells to execute phagocytosis (Sevigny, J., et al. (2016). *Nature* 537(7618): 50-56), this approach targets a conserved microbial pathway to induce phagocytosis and immune stimulation.

[0366] Bispecific antibodies were generated with one arm targeting Dectin-1 and the other arm targeting amyloid beta (based on the variable domain sequences of aducanumab or lecanemab). Aducanumab variable domain sequences are as follows. VH: QVQLVESGGGVVQPGRSLRLSCAASGFAFSSYGMHWVRQAPGKGLEWVAVIWFDGTKKYYTD SVKGRFTISRDNSKNTLYLQMNTLRAEDTAVYYCARDRGIGARRGPYYMDVWGKGTTVTVSS (SEQ ID NO:145); VL: DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGS GTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIK (SEQ ID NO:146). Lecanemab variable

domain sequences are as follows. VH:
EVQLVESGGGLVQPGGSLRLSCSASGFTFSSFGMHWVRQAPGKGLEWVAYISSGSSTIYYGDTV
KGRFTISRDNAKNSLFLQMSSLRAEDTAVYYCAREGGYYYGRSYYTMDYWGQGTTVTVSS
(SEQ ID NO:147); VL:
DVVMTQSPLSLPVTPGAPASISCRSSQSIVHSNGNTYLEWYLQKPGQSPKLLIYKVSNRFSGVPDR
FSGSGSGTDFTLRISRVEAEDVGIYYCFQGSHVPPTFGPGTKLEIK (SEQ ID NO:148).

Example 16: Tuning of myeloid engagers

Materials and Methods

Phagocytosis/depletion

[0367] Cells were resuspended at 2M/mL in RPMI + 10% ultra low IgG FBS + 1X Pen/Strep, and 100 uL were plated for 200,000 cells/well. 100 uL of antibody dilutions were added to each well. Plates were incubated overnight at 37°C for 20-24 hours. Cells were then spun down, and supernatants were transferred to assess cytokine production for IFNg, IL10, IL6, and TNFa. IFNg levels assessed by ELISA (Invitrogen cat# 50-173-28).

Flow cytometry

[0368] Cells were resuspended in 150 uL FACS Buffer to wash, then spun down and resuspended in BD Fc Block diluted 1:50 and efluor 506 viability dye diluted 1:1000, 50 uL/well (30 min on ice). Cells were then spun down and resuspended in 100 ul of antibody dilutions. Cells were then incubated for 30 minutes on ice in dark and washed with FACS Buffer. Cells were then resuspended in 100 uL of FACS Buffer, and 30,000 cell events were acquired on Cytoflex.

CD16a ELISA

[0369] Plate was coated with recombinant huCD16a using 100 µL @ 1.0 µg/mL. Using a plate washer, plate(s) were washed with 300 µL/well three (3) times using the Wash Buffer. Plate(s) were blocked with 300 µL/well of Blocking Buffer, then sealed and incubated at room temperature (RT) on a plate shaker at ~ 200 rpm for 90 minutes. After blocking, plate(s) were washed with 300 µL/well three (3) times using the Wash Buffer. 100 µL of sample was added from the dilution plate to the appropriate wells on the assay plate, then plate(s) were sealed and incubated at RT on a plate shaker ~ 200 rpm for 60 ± 5 minutes. Detection antibody (Jackson ImmunoResearch Peroxidase AffiniPure F(ab')2 Fragment Goat Anti-Human IgG) was diluted 1:8,000 in blocking buffer. Samples were incubated for 1 hour, then plate(s) were washed with 300 µL/well three (3) times using the Wash Buffer. Diluted detection antibody was added at 100 µL/well to all wells. Plate(s) were sealed and incubated at RT on a plate shaker ~ 200 rpm for 60 ± 5 minutes. After the 1-hour detection antibody incubation, plate(s) were washed with 300 µL/well three (3) times using the Wash Buffer. KPL SureBlueTM TMB Substrate was added at 100 µL/well, and plates were incubated without shaking at RT for eight minutes. 1N sulfuric acid was added

at 100 µL/well to stop the reaction. Plate(s) were read at 450 nm with a 630 nm reference reading on an ELISA plate reader within 15 minutes of stopping reaction (timed from the addition to last row of the last plate).

Results

[0370] The functional activities of multispecific (*e.g.*, bispecific) binding molecules as described herein are the result of the binding affinity/specificity of each antigen binding domain as well as the Fc region.

[0371] For example, the myeloid cell engager shown in **FIG. 67** has 2 arms and an Fc region (arm 3). In this exemplary molecule, Arm 1 binds to the myeloid receptor Dectin-1, in which binding affinity can be modulated. Arm 2 binds to target of choice, and here epitope and affinity can be selected. Arm 3 is the Fc isotype (*e.g.*, hIgG1 inert, hIgG4, hIgG1 and variants that alter Fc gamma receptor binding). The combination of these 3 arms affects the binding preference of the myeloid engager as well as its immune-modulating activity. Depending on the target(s) of interest and/or desired functional activities, modulating the binding affinity of each arm and/or properties of the Fc region (*e.g.*, Fc gamma receptor binding) could be desirable.

[0372] In order to tune the properties of anti-Dectin-1 clone 2M24 and any multispecific (*e.g.*, bispecific) binding molecules comprising the 2M24 antigen binding domain, a series of 2M24 variants were constructed. Certain residues in the heavy and light CDRs of dectin-1 clone 2M24 were changed to generate affinity variants. These variants were expressed and purified as Fabs. Fab binding to recombinant Dectin-1 were tested, and the dissociation rate were determined.

[0373] To test affinity variants, the dissociation rate of 2M24 fab variants to recombinant dectin-1 protein was assayed via biosensor (Octet; **FIG. 68A**). Recombinant human-Dectin-1 mouse Fc fusion was captured first using anti-mouse IgG octet biosensors. Captured human-Dectin-1 mouse Fc fusion was then dipped into 100 nM of 2M24 Fab variants, and this association step was monitored for 120 seconds. Biosensor tip was them moved into buffer to monitor dissociation step for 120 seconds. The dissociation rate was fitted from these data (**FIG. 68B**). Koff rates and variable domain sequences for the variants tested as shown in Table 2.

Table 2. Binding properties and sequences of 2M24 variants.

Clone name	**K off rate**	**VH**	**VL**
2M24A.1 hFab	6.37E-03	QVQLVQSGAEVKKPGASVKVSCKSS GYTFTDYYIHWVRQAPGQGLEWMG WINPNSGDTNYAQKFQGRITMTRDT SISTAYLELSRLRSDDTAVFYCARNS GSYSFGYWGQGTLVTVSS (SEQ ID NO:62)	DIQMTQSPSSVSASVGDRVTITC RASQGISSWLAWYQQKPGKAPK LLIFGASSLQSGVPSRFSGSGSGT DFTLTVSSLQPEDFATYYCQQAY SFPFTFGPGTKVDIE (SEQ ID NO:64)
2M24A.1 hFab	4.42E-03	QVQLVQSGAEVKKPGASVKVSCKSS GYTFTDYYIHWVRQAPGQGLEWMG	DIQMTQSPSSVSASVGDRVTITC RASQGISSWLAWYQQKPGKAPK

		WINPNSGDTNYAQKFQGRITMTRDT SISTAYLELSRLRSDDTAVFYCARNS GSYSFGYWGQGTLVTVSS (SEQ ID NO:62)	LLIFGASSLQSGVPSRFSGSGSGT DFTLTVSSLQPEDFATYYCQQAY SFPFTFGPGTKVDIE (SEQ ID NO:64)
2M24A.1 hFab	3.64E-03	QVQLVQSGAEVKKPGASVKVSCKSS GYTFTDYYIHWVRQAPGQGLEWMG WINPNSGDTNYAQKFQGRITMTRDT SISTAYLELSRLRSDDTAVFYCARNS GSYSFGYWGQGTLVTVSS (SEQ ID NO:62)	DIQMTQSPSSVSASVGDRVTITC RASQGISSWLAWYQQKPGKAPK LLIFGASSLQSGVPSRFSGSGSGT DFTLTVSSLQPEDFATYYCQQAY SFPFTFGPGTKVDIE (SEQ ID NO:64)
2M24A.1 hFab	1.20E-03	QVQLVQSGAEVKKPGASVKVSCKSS GYTFTDYYIHWVRQAPGQGLEWMG WINPNSGDTNYAQKFQGRITMTRDT SISTAYLELSRLRSDDTAVFYCARNS GSYSFGYWGQGTLVTVSS (SEQ ID NO:62)	DIQMTQSPSSVSASVGDRVTITC RASQGISSWLAWYQQKPGKAPK LLIFGASSLQSGVPSRFSGSGSGT DFTLTVSSLQPEDFATYYCQQAY SFPFTFGPGTKVDIE (SEQ ID NO:64)
2M24A.1.1 hFab	**2.69E-02**	QVQLVQSGAEVKKPGASVKVSCKSS GYTFT**A**YYIHWVRQAPGQGLEWMG WINPNSGDTNYAQKFQGRITMTRDT SISTAYLELSRLRSDDTAVFYCARNS GSYSFGYWGQGTLVTVSS (SEQ ID NO:82)	DIQMTQSPSSVSASVGDRVTITC RASQGISSWLAWYQQKPGKAPK LLIFGASSLQSGVPSRFSGSGSGT DFTLTVSSLQPEDFATYYCQQA**A** SFPFTFGPGTKVDIE (SEQ ID NO:94)
2M24A.1.2 hFab	**2.96E-02**	QVQLVQSGAEVKKPGASVKVSCKSS GYTFTDYYIHWVRQAPGQGLEWMG WINPNSG**A**TNYAQKFQGRITMTRDT SISTAYLELSRLRSDDTAVFYCARNS GSYSFGYWGQGTLVTVSS (SEQ ID NO:83)	DIQMTQSPSSVSASVGDRVTITC RASQGISSWLAWYQQKPGKAPK LLIFGASSLQSGVPSRFSGSGSGT DFTLTVSSLQPEDFATYYCQQA**A** SFPFTFGPGTKVDIE (SEQ ID NO:94)
2M24A.1.3 hFab	9.12E-03	QVQLVQSGAEVKKPGASVKVSCKSS GYTFTDYYIHWVRQAPGQGLEWMG WINPNSGDTNYAQKFQGRITMTRDT SISTAYLELSRLRSDDTAVFYCAR**A**S GSYSFGYWGQGTLVTVSS (SEQ ID NO:84)	DIQMTQSPSSVSASVGDRVTITC RASQGISSWLAWYQQKPGKAPK LLIFGASSLQSGVPSRFSGSGSGT DFTLTVSSLQPEDFATYYCQQA**A** SFPFTFGPGTKVDIE (SEQ ID NO:94)
2M24A.1.4 hFab	**1.03E-02**	QVQLVQSGAEVKKPGASVKVSCKSS GYTFTDYYIHWVRQAPGQGLEWMG WINPNSGDTNYAQKFQGRITMTRDT SISTAYLELSRLRSDDTAVFYCARNS G**S**ASFGYWGQGTLVTVSS (SEQ ID NO:85)	DIQMTQSPSSVSASVGDRVTITC RASQGISSWLAWYQQKPGKAPK LLIFGASSLQSGVPSRFSGSGSGT DFTLTVSSLQPEDFATYYCQQA**A** SFPFTFGPGTKVDIE (SEQ ID NO:94)
2M24A.1.5 hFab	**2.47E-02**	QVQLVQSGAEVKKPGASVKVSCKSS GYTFTDYYIHWVRQAPGQGLEWMG WINPNSGDTNYAQKFQGRITMTRDT SISTAYLELSRLRSDDTAVFYCARNS GSYSFGYWGQGTLVTVSS (SEQ ID NO:62)	DIQMTQSPSSVSASVGDRVTITC RASQGISSWLAWYQQKPGKAPK LLIFGASSLQSGVPSRFSGSGSGT DFTLTVSSLQPEDFATYYCQQA**A** SFPFTFGPGTKVDIE (SEQ ID NO:94)
2M24A.1.6 hFab	5.59E-03	QVQLVQSGAEVKKPGASVKVSCKSS GYTFT**A**YYIHWVRQAPGQGLEWMG WINPNSGDTNYAQKFQGRITMTRDT SISTAYLELSRLRSDDTAVFYCARNS GSYSFGYWGQGTLVTVSS (SEQ ID NO:82)	DIQMTQSPSSVSASVGDRVTITC RASQGISSWLAWYQQKPGKAPK LLIFGASSLQSGVPSRFSGSGSGT DFTLTVSSLQPEDFATYYCQQA**F** SFPFTFGPGTKVDIE (SEQ ID NO:95)
2M24A.1.7 hFab	6.36E-03	QVQLVQSGAEVKKPGASVKVSCKSS GYTFTDYYIHWVRQAPGQGLEWMG	DIQMTQSPSSVSASVGDRVTITC RASQGISSWLAWYQQKPGKAPK

		WINPNSGATNYAQKFQGRITMTRDT SISTAYLELSRLRSDDTAVFYCARNS GSYSFGYWGQGTLVTVSS (SEQ ID NO:83)	LLIFGASSLQSGVPSRFSGSGSGT DFTLTVSSLQPEDFATYYCQQAF SFPFTFGPGTKVDIE (SEQ ID NO:95)
2M24A.1.8 hFab	**2.16E-01**	QVQLVQSGAEVKKPGASVKVSCKSS GYTFTDYYIHWVRQAPGQGLEWMG WINPNSGDTNYAQKFQGRITMTRDT SISTAYLELSRLRSDDTAVFYCARAS GSYSFGYWGQGTLVTVSS (SEQ ID NO:84)	DIQMTQSPSSVSASVGDRVTITC RASQGISSWLAWYQQKPGKAPK LLIFGASSLQSGVPSRFSGSGSGT DFTLTVSSLQPEDFATYYCQQAF SFPFTFGPGTKVDIE (SEQ ID NO:95)
2M24A.1.9 hFab	**2.53E-01**	QVQLVQSGAEVKKPGASVKVSCKSS GYTFTDYYIHWVRQAPGQGLEWMG WINPNSGDTNYAQKFQGRITMTRDT SISTAYLELSRLRSDDTAVFYCARNS GSASFGYWGQGTLVTVSS (SEQ ID NO:85)	DIQMTQSPSSVSASVGDRVTITC RASQGISSWLAWYQQKPGKAPK LLIFGASSLQSGVPSRFSGSGSGT DFTLTVSSLQPEDFATYYCQQAF SFPFTFGPGTKVDIE (SEQ ID NO:95)
2M24A.1.10 hFab	3.85E-03	QVQLVQSGAEVKKPGASVKVSCKSS GYTFTDYYIHWVRQAPGQGLEWMG WINPNSGDTNYAQKFQGRITMTRDT SISTAYLELSRLRSDDTAVFYCARNS GSYSFGYWGQGTLVTVSS (SEQ ID NO:62)	DIQMTQSPSSVSASVGDRVTITC RASQGISSWLAWYQQKPGKAPK LLIFGASSLQSGVPSRFSGSGSGT DFTLTVSSLQPEDFATYYCQQAF SFPFTFGPGTKVDIE (SEQ ID NO:95)
2M24A.1.11 hFab	3.36E-03	QVQLVQSGAEVKKPGASVKVSCKSS GYTFTAYYIHWVRQAPGQGLEWMG WINPNSGDTNYAQKFQGRITMTRDT SISTAYLELSRLRSDDTAVFYCARNS GSYSFGYWGQGTLVTVSS (SEQ ID NO:82)	DIQMTQSPSSVSASVGDRVTITC RASQGISSWLAWYQQKPGKAPK LLIFGASSLQSGVPSRFSGSGSGT DFTLTVSSLQPEDFATYYCQQAY SFPFTFGPGTKVDIE (SEQ ID NO:64)
2M24A.1.12 hFab	3.96E-03	QVQLVQSGAEVKKPGASVKVSCKSS GYTFTDYYIHWVRQAPGQGLEWMG WINPNSGATNYAQKFQGRITMTRDT SISTAYLELSRLRSDDTAVFYCARNS GSYSFGYWGQGTLVTVSS (SEQ ID NO:83)	DIQMTQSPSSVSASVGDRVTITC RASQGISSWLAWYQQKPGKAPK LLIFGASSLQSGVPSRFSGSGSGT DFTLTVSSLQPEDFATYYCQQAY SFPFTFGPGTKVDIE (SEQ ID NO:64)
2M24A.1.13 hFab	**2.42E-01**	QVQLVQSGAEVKKPGASVKVSCKSS GYTFTDYYIHWVRQAPGQGLEWMG WINPNSGDTNYAQKFQGRITMTRDT SISTAYLELSRLRSDDTAVFYCARAS GSYSFGYWGQGTLVTVSS (SEQ ID NO:84)	DIQMTQSPSSVSASVGDRVTITC RASQGISSWLAWYQQKPGKAPK LLIFGASSLQSGVPSRFSGSGSGT DFTLTVSSLQPEDFATYYCQQAY SFPFTFGPGTKVDIE (SEQ ID NO:64)
2M24A.1.14 hFab	**1.56E-01**	QVQLVQSGAEVKKPGASVKVSCKSS GYTFTDYYIHWVRQAPGQGLEWMG WINPNSGDTNYAQKFQGRITMTRDT SISTAYLELSRLRSDDTAVFYCARNS GSASFGYWGQGTLVTVSS (SEQ ID NO:85)	DIQMTQSPSSVSASVGDRVTITC RASQGISSWLAWYQQKPGKAPK LLIFGASSLQSGVPSRFSGSGSGT DFTLTVSSLQPEDFATYYCQQAY SFPFTFGPGTKVDIE (SEQ ID NO:64)
2M24A.1.15	**2.39E-02**	QVQLVQSGAEVKKPGASVKVSCKSS GYTFTDYYIHWVRQAPGQGLEWMG WINPNSGDTNYAQKFQGRITMTRDT SISTAYLELSRLRSDDTAVFYCAANS GSYSFGYWGQGTLVTVSS (SEQ ID NO:86)	DIQMTQSPSSVSASVGDRVTITC RASQGISSWLAWYQQKPGKAPK LLIFGASSLQSGVPSRFSGSGSGT DFTLTVSSLQPEDFATYYCQQAY SFPFTFGPGTKVDIE (SEQ ID NO:64)
2M24A.1.16	1.61E-03	QVQLVQSGAEVKKPGASVKVSCKSS GYTFTDYYIHWVRQAPGQGLEWMG	DIQMTQSPSSVSASVGDRVTITC RASQGISSWLAWYQQKPGKAPK

		WINPNSGDTNYAQKFQGRITMTRDT SISTAYLELSRLRSDDTAVFYCARNA GSYSFGYWGQGTLVTVSS (SEQ ID NO:87)	LLIFGASSLQSGVPSRFSGSGSGT DFTLTVSSLQPEDFATYYCQQAY SFPFTFGPGTKVDIE (SEQ ID NO:64)
2M24A.1.17	6.45E-04	QVQLVQSGAEVKKPGASVKVSCKSS GYTFTDYYIHWVRQAPGQGLEWMG WINPNSGDTNYAQKFQGRITMTRDT SISTAYLELSRLRSDDTAVFYCARNS ASYSFGYWGQGTLVTVSS (SEQ ID NO:88)	DIQMTQSPSSVSASVGDRVTITC RASQGISSWLAWYQQKPGKAPK LLIFGASSLQSGVPSRFSGSGSGT DFTLTVSSLQPEDFATYYCQQAY SFPFTFGPGTKVDIE (SEQ ID NO:64)
2M24A.1.18	1.92E-03	QVQLVQSGAEVKKPGASVKVSCKSS GYTFTDYYIHWVRQAPGQGLEWMG WINPNSGDTNYAQKFQGRITMTRDT SISTAYLELSRLRSDDTAVFYCARNS GAYSFGYWGQGTLVTVSS (SEQ ID NO:89)	DIQMTQSPSSVSASVGDRVTITC RASQGISSWLAWYQQKPGKAPK LLIFGASSLQSGVPSRFSGSGSGT DFTLTVSSLQPEDFATYYCQQAY SFPFTFGPGTKVDIE (SEQ ID NO:64)
2M24A.1.19	5.94E-03	QVQLVQSGAEVKKPGASVKVSCKSS GYTFTDYYIHWVRQAPGQGLEWMG WINPNSGDTNYAQKFQGRITMTRDT SISTAYLELSRLRSDDTAVFYCARNS GSYAFGYWGQGTLVTVSS (SEQ ID NO:90)	DIQMTQSPSSVSASVGDRVTITC RASQGISSWLAWYQQKPGKAPK LLIFGASSLQSGVPSRFSGSGSGT DFTLTVSSLQPEDFATYYCQQAY SFPFTFGPGTKVDIE (SEQ ID NO:64)
2M24A.1.20	**3.60E-02**	QVQLVQSGAEVKKPGASVKVSCKSS GYTFTDYYIHWVRQAPGQGLEWMG WINPNSGDTNYAQKFQGRITMTRDT SISTAYLELSRLRSDDTAVFYCARNS GSYSAGYWGQGTLVTVSS (SEQ ID NO:91)	DIQMTQSPSSVSASVGDRVTITC RASQGISSWLAWYQQKPGKAPK LLIFGASSLQSGVPSRFSGSGSGT DFTLTVSSLQPEDFATYYCQQAY SFPFTFGPGTKVDIE (SEQ ID NO:64)
2M24A.1.21	2.38E-03	QVQLVQSGAEVKKPGASVKVSCKSS GYTFTDYYIHWVRQAPGQGLEWMG WINPNSGDTNYAQKFQGRITMTRDT SISTAYLELSRLRSDDTAVFYCARNS GSYSFAYWGQGTLVTVSS (SEQ ID NO:92)	DIQMTQSPSSVSASVGDRVTITC RASQGISSWLAWYQQKPGKAPK LLIFGASSLQSGVPSRFSGSGSGT DFTLTVSSLQPEDFATYYCQQAY SFPFTFGPGTKVDIE (SEQ ID NO:64)
2M24A.1.22	3.32E-03	QVQLVQSGAEVKKPGASVKVSCKSS GYTFTDYYIHWVRQAPGQGLEWMG WINPNSGDTNYAQKFQGRITMTRDT SISTAYLELSRLRSDDTAVFYCARNS GSYSFGAWGQGTLVTVSS (SEQ ID NO:93)	DIQMTQSPSSVSASVGDRVTITC RASQGISSWLAWYQQKPGKAPK LLIFGASSLQSGVPSRFSGSGSGT DFTLTVSSLQPEDFATYYCQQAY SFPFTFGPGTKVDIE (SEQ ID NO:64)
2M24A.1.23	5.36E-03	QVQLVQSGAEVKKPGASVKVSCKSS GYTFTDYYIHWVRQAPGQGLEWMG WINPNSGDTNYAQKFQGRITMTRDT SISTAYLELSRLRSDDTAVFYCARNS GSYSFGYWGQGTLVTVSS (SEQ ID NO:62)	DIQMTQSPSSVSASVGDRVTITC RASQGISSWLAWYQQKPGKAPK LLIFGASSLQSGVPSRFSGSGSGT DFTLTVSSLQPEDFATYYCAQAY SFPFTFGPGTKVDIE (SEQ ID NO:96)
2M24A.1.24	**1.05E-02**	QVQLVQSGAEVKKPGASVKVSCKSS GYTFTDYYIHWVRQAPGQGLEWMG WINPNSGDTNYAQKFQGRITMTRDT SISTAYLELSRLRSDDTAVFYCARNS GSYSFGYWGQGTLVTVSS (SEQ ID NO:62)	DIQMTQSPSSVSASVGDRVTITC RASQGISSWLAWYQQKPGKAPK LLIFGASSLQSGVPSRFSGSGSGT DFTLTVSSLQPEDFATYYCQAAY SFPFTFGPGTKVDIE (SEQ ID NO:97)
2M24A.1.25	4.92E-03	QVQLVQSGAEVKKPGASVKVSCKSS GYTFTDYYIHWVRQAPGQGLEWMG	DIQMTQSPSSVSASVGDRVTITC RASQGISSWLAWYQQKPGKAPK

		WINPNSGDTNYAQKFQGRITMTRDT SISTAYLELSRLRSDDTAVFYCARNS GSYSFGYWGQGTLVTVSS (SEQ ID NO:62)	LLIFGASSLQSGVPSRFSGSGSGT DFTLTVSSLQPEDFATYYCQQAY AFPFTFGPGTKVDIE (SEQ ID NO:98)
2M24A.1.26	**6.87E-02**	QVQLVQSGAEVKKPGASVKVSCKSS GYTFTDYYIHWVRQAPGQGLEWMG WINPNSGDTNYAQKFQGRITMTRDT SISTAYLELSRLRSDDTAVFYCARNS GSYSFGYWGQGTLVTVSS (SEQ ID NO:62)	DIQMTQSPSSVSASVGDRVTITC RASQGISSWLAWYQQKPGKAPK LLIFGASSLQSGVPSRFSGSGSGT DFTLTVSSLQPEDFATYYCQQAY SAPFTFGPGTKVDIE (SEQ ID NO:99)
2M24A.1.27	7.92E-03	QVQLVQSGAEVKKPGASVKVSCKSS GYTFTDYYIHWVRQAPGQGLEWMG WINPNSGDTNYAQKFQGRITMTRDT SISTAYLELSRLRSDDTAVFYCARNS GSYSFGYWGQGTLVTVSS (SEQ ID NO:62)	DIQMTQSPSSVSASVGDRVTITC RASQGISSWLAWYQQKPGKAPK LLIFGASSLQSGVPSRFSGSGSGT DFTLTVSSLQPEDFATYYCQQAY SFAFTFGPGTKVDIE (SEQ ID NO:100)
2M24A.1.28	**4.79E-02**	QVQLVQSGAEVKKPGASVKVSCKSS GYTFTDYYIHWVRQAPGQGLEWMG WINPNSGDTNYAQKFQGRITMTRDT SISTAYLELSRLRSDDTAVFYCARNS GSYSFGYWGQGTLVTVSS (SEQ ID NO:62)	DIQMTQSPSSVSASVGDRVTITC RASQGISSWLAWYQQKPGKAPK LLIFGASSLQSGVPSRFSGSGSGT DFTLTVSSLQPEDFATYYCQQAY SFPATFGPGTKVDIE (SEQ ID NO:101)
2M24A.1.29	7.46E-03	QVQLVQSGAEVKKPGASVKVSCKSS GYTFTDYYIHWVRQAPGQGLEWMG WINPNSGDTNYAQKFQGRITMTRDT SISTAYLELSRLRSDDTAVFYCARNS GSYSFGYWGQGTLVTVSS (SEQ ID NO:62)	DIQMTQSPSSVSASVGDRVTITC RASQGISSWLAWYQQKPGKAPK LLIFGASSLQSGVPSRFSGSGSGT DFTLTVSSLQPEDFATYYCQQAY SFPFAFGPGTKVDIE (SEQ ID NO:102)

[0374] Fc gamma receptors can play a role in the overall activity of myeloid engager. To demonstrate this, 2M24xCD20 bispecific antibodies with KIF (glycosylation modified) treated hIgG1 Fc were compared to those with hIgG4 Fc in a B cell depletion assay using PMBC from 2 donors (**FIGS. 69A & 69B**). Human IgG4 has different Fc gamma receptor affinity and specificity compared to hIgG1 KIF (glycosylation modified), and these differences resulted in less immune-based activity. These results demonstrate that Fc modulation can decrease activity of myeloid engagers.

[0375] Enhancing Fc gamma receptor binding by the Fc can be achieved through glycosylation modification such as removing the fucose sugar, and/or mutation specific residues in hIgG1 CH2 domains. These methods have been described and tested in the clinic; *see, e.g.,* Liu, R. *et al.* (2020) *Antibodies (Basel)* 9:64. This was monitored by looking at the binding of Fc gamma receptor CD16a F variant via ELISA. These modified bispecific antibodies were compared to parental hIgG1 based line, and hIgG1 non-fucosylated (**FIGS. 70A-70D**). These results demonstrated that Fc modulation can also increase activity of myeloid engagers.

[0376] Another set of mutations were introduced into the 2M24 clone to revert certain positions back to human germline residues. Fab fragments with these mutations were also tested for binding affinity, and the results are shown in Tables 3 and 4A (variable domain sequences for each molecule are provided in

Table 4B). These results demonstrate that anti-Dectin-1 antigen binding domains comprising these mutations retained high affinity binding for hDectin-1.

Table 3. Germline reversions of clone 2M24 (heavy chain).

Clone	Mutation(s)	K dis (1/s)	K dis (1/s)	K dis (1/s)	Ave	Stdev
2M24A.1 parent (Fab)	-	6.04E-03	1.52E-03	2.24E-03	3.27E-03	2.43E-03
2M24A.23 hFab H1	I68V, L81M, F94Y	8.41E-03	1.43E-03	2.04E-03	3.96E-03	3.87E-03
2M24A.24 hFab H2	S24A, I34M, I68V, L81M, F94Y	8.26E-03	6.16E-04	1.50E-03	3.46E-03	4.18E-03
2M24A.25 hFab H3	S24A, I68V, L81M, F94Y	7.65E-03	1.32E-03	2.14E-03	3.70E-03	3.44E-03
2M24A.26 hFab H4	I34M, I68V, L81M, F94Y	5.30E-03	1.02E-03	1.60E-03	2.64E-03	2.32E-03
2M24A.27 hFab H5	S24A, D31G, I34M, I68V, L81M, F94Y	6.24E-03	1.95E-03	3.20E-03	3.80E-03	2.21E-03
2M24A.28 hFab H6	S24A, I34M, D57G, I68V, L81M, F94Y	4.12E-03	9.95E-04	1.51E-03	2.21E-03	1.68E-03
2M24A.29 hFab H7	S24A, D31G, I34M, D57G, I68V, L81M, F94Y	5.56E-03	2.04E-03	2.67E-03	3.42E-03	1.88E-03

Table 4A. Germline reversions of clone 2M24 (light chain).

Clone	Mutation(s)	K dis (1/s)	K dis (1/s)	K dis (1/s)	Ave	Stdev
2M24A.1 parent (Fab)	-	4.39E-03	1.67E-03	1.72E-03	2.59E-03	1.56E-03
2M24A.30 hFab L1	V75I	6.31E-03	2.08E-03	2.13E-03	3.51E-03	2.43E-03

2M24A.31 hFab L2	F49Y, V75I	6.35E-03	2.36E-03	2.39E-03	3.70E-03	2.30E-03
2M24A.32 hFab L3	G50A, V75I	6.71E-03	2.23E-03	2.33E-03	3.76E-03	2.56E-03
2M24A.33 hFab L4	F49Y, G50A, V75I	6.15E-03	2.78E-03	3.14E-03	4.02E-03	1.85E-03

Table 4B. Germline reversions of clone 2M24 (variable domains).

Name	**Ave K dis (1/s) (n=3)**	**Heavy**	**Light**
2M24 Parental	3.27E-03	QVQLVQSGAEVKKPGASVKVSCK SSGYTFT**D**YY**I**HWVRQAPGQGLE WMGWINPNSG**D**TNYAQKFQGR**I**T MTRDTSISTAYLELSRLRSDDTAV **F**YCARNSGSYSFGYWGQGTLVTV SS (SEQ ID NO:62)	DIQMTQSPSSVSASVGDRVTI TCRASQGISSWLAWYQQKP GKAPKLLIFGASSLQSGVPSR FSGSGSGTDFTLTVSSLQPED FATYYCQQAYSFPFTFGPGT KVDIE (SEQ ID NO:64)
2M24.H1	3.96E-03	QVQLVQSGAEVKKPGASVKVSCK SSGYTFTDYYIHWVRQAPGQGLE WMGWINPNSGDTNYAQKFQGRV TMTRDTSISTAYMELSRLRSDDTA VYYCARNSGSYSFGYWGQGTLVT VSS (SEQ ID NO:103)	DIQMTQSPSSVSASVGDRVTI TCRASQGISSWLAWYQQKP GKAPKLLIFGASSLQSGVPSR FSGSGSGTDFTLTVSSLQPED FATYYCQQAYSFPFTFGPGT KVDIE (SEQ ID NO:64)
2M24.H2	3.46E-03	QVQLVQSGAEVKKPGASVKVSCK ASGYTFTDYYMHWVRQAPGQGL EWMGWINPNSGDTNYAQKFQGR VTMTRDTSISTAYMELSRLRSDDT AVYYCARNSGSYSFGYWGQGTLV TVSS (SEQ ID NO:104)	DIQMTQSPSSVSASVGDRVTI TCRASQGISSWLAWYQQKP GKAPKLLIFGASSLQSGVPSR FSGSGSGTDFTLTVSSLQPED FATYYCQQAYSFPFTFGPGT KVDIE (SEQ ID NO:64)
2M24.H3	3.70E-03	QVQLVQSGAEVKKPGASVKVSCK ASGYTFTDYYIHWVRQAPGQGLE WMGWINPNSGDTNYAQKFQGRV TMTRDTSISTAYMELSRLRSDDTA VYYCARNSGSYSFGYWGQGTLVT VSS (SEQ ID NO:105)	DIQMTQSPSSVSASVGDRVTI TCRASQGISSWLAWYQQKP GKAPKLLIFGASSLQSGVPSR FSGSGSGTDFTLTVSSLQPED FATYYCQQAYSFPFTFGPGT KVDIE (SEQ ID NO:64)
2M24.H4	2.64E-03	QVQLVQSGAEVKKPGASVKVSCK SSGYTFTDYYMHWVRQAPGQGLE WMGWINPNSGDTNYAQKFQGRV TMTRDTSISTAYMELSRLRSDDTA VYYCARNSGSYSFGYWGQGTLVT VSS (SEQ ID NO:106)	DIQMTQSPSSVSASVGDRVTI TCRASQGISSWLAWYQQKP GKAPKLLIFGASSLQSGVPSR FSGSGSGTDFTLTVSSLQPED FATYYCQQAYSFPFTFGPGT KVDIE (SEQ ID NO:64)
2M24.H5	3.80E-03	QVQLVQSGAEVKKPGASVKVSCK ASGYTFTGYYMHWVRQAPGQGL EWMGWINPNSGDTNYAQKFQGR VTMTRDTSISTAYMELSRLRSDDT AVYYCARNSGSYSFGYWGQGTLV TVSS (SEQ ID NO:107)	DIQMTQSPSSVSASVGDRVTI TCRASQGISSWLAWYQQKP GKAPKLLIFGASSLQSGVPSR FSGSGSGTDFTLTVSSLQPED FATYYCQQAYSFPFTFGPGT KVDIE (SEQ ID NO:64)
2M24.H6	2.21E-03	QVQLVQSGAEVKKPGASVKVSCK ASGYTFTDYYMHWVRQAPGQGL EWMGWINPNSGGTNYAQKFQGR VTMTRDTSISTAYMELSRLRSDDT	DIQMTQSPSSVSASVGDRVTI TCRASQGISSWLAWYQQKP GKAPKLLIFGASSLQSGVPSR FSGSGSGTDFTLTVSSLQPED

		AVYYCARNSGSYSFGYWGQGTLV TVSS (SEQ ID NO:108)	FATYYCQQAYSFPFTFGPGT KVDIE (SEQ ID NO:64)
2M24.H7	3.42E-03	QVQLVQSGAEVKKPGASVKVSCK ASGYTFTGYYMHWVRQAPGQGL EWMGWINPNSGGTNYAQKFQGR VTMTRDTSISTAYMELSRLRSDDT AVYYCARNSGSYSFGYWGQGTLV TVSS (SEQ ID NO:109)	DIQMTQSPSSVSASVGDRVTI TCRASQGISSWLAWYQQKP GKAPKLLIFGASSLQSGVPSR FSGSGSGTDFTLTVSSLQPED FATYYCQQAYSFPFTFGPGT KVDIE (SEQ ID NO:64)
2M24 Parental	2.59E-03	QVQLVQSGAEVKKPGASVKVSCK SSGYTFTDYYIHWVRQAPGQGLE WMGWINPNSGDTNYAQKFQGRIT MTRDTSISTAYLELSRLRSDDTAV FYCARNSGSYSFGYWGQGTLVTV SS (SEQ ID NO:62)	DIQMTQSPSSVSASVGDRVTI TCRASQGISSWLAWYQQKP GKAPKLLI**F**GASSLQSGVPSR FSGSGSGTDFTLT**V**SSLQPED FATYYCQQAYSFPFTFGPGT KVDIE (SEQ ID NO:64)
2M24.L1	3.51E-03	QVQLVQSGAEVKKPGASVKVSCK SSGYTFTDYYIHWVRQAPGQGLE WMGWINPNSGDTNYAQKFQGRIT MTRDTSISTAYLELSRLRSDDTAV FYCARNSGSYSFGYWGQGTLVTV SS (SEQ ID NO:62)	DIQMTQSPSSVSASVGDRVTI TCRASQGISSWLAWYQQKP GKAPKLLIFGASSLQSGVPSR FSGSGSGTDFTLTISSLQPEDF ATYYCQQAYSFPFTFGPGTK VDIE (SEQ ID NO:110)
2M24.L2	3.70E-03	QVQLVQSGAEVKKPGASVKVSCK SSGYTFTDYYIHWVRQAPGQGLE WMGWINPNSGDTNYAQKFQGRIT MTRDTSISTAYLELSRLRSDDTAV FYCARNSGSYSFGYWGQGTLVTV SS (SEQ ID NO:62)	DIQMTQSPSSVSASVGDRVTI TCRASQGISSWLAWYQQKP GKAPKLLIYGASSLQSGVPSR FSGSGSGTDFTLTISSLQPEDF ATYYCQQAYSFPFTFGPGTK VDIE (SEQ ID NO:111)
2M24.L3	3.76E-03	QVQLVQSGAEVKKPGASVKVSCK SSGYTFTDYYIHWVRQAPGQGLE WMGWINPNSGDTNYAQKFQGRIT MTRDTSISTAYLELSRLRSDDTAV FYCARNSGSYSFGYWGQGTLVTV SS (SEQ ID NO:62)	DIQMTQSPSSVSASVGDRVTI TCRASQGISSWLAWYQQKP GKAPKLLIFAASSLQSGVPSR FSGSGSGTDFTLTISSLQPEDF ATYYCQQAYSFPFTFGPGTK VDIE (SEQ ID NO:112)
2M24.L4	4.02E-03	QVQLVQSGAEVKKPGASVKVSCK SSGYTFTDYYIHWVRQAPGQGLE WMGWINPNSGDTNYAQKFQGRIT MTRDTSISTAYLELSRLRSDDTAV FYCARNSGSYSFGYWGQGTLVTV SS (SEQ ID NO:62)	DIQMTQSPSSVSASVGDRVTI TCRASQGISSWLAWYQQKP GKAPKLLIYAASSLQSGVPSR FSGSGSGTDFTLTISSLQPEDF ATYYCQQAYSFPFTFGPGTK VDIE (SEQ ID NO:113)

Example 17: Tuning of binding affinity of myeloid engagers to human Dectin-1

[0377] As illustrated in **FIG. 67**, myeloid engagers of the present disclosure can be tuned by modulating the functional properties of three components: the variable domains that bind Dectin-1 (Arm 1), the variable domains that bind a target of interest (Arm 2), and the Fc region that engages with myeloid cells expressing appropriate Fc receptors on their cell surface. This Example describes the introduction of alanine substitutions at various positions in the 2M24 variable domains. The goal of these experiments is to identify residues important for binding and provide variant binding domains with a range of affinities. For example, it may be beneficial in some cases to reduce binding affinity of Arm 1 to human Dectin-1 or

binding avidity of Arm 1 and the Fc region to myeloid cells, *e.g.*, depending on the binding properties of Arm 2 to the target of interest.

[0378] Variant binding domains were generated, and binding affinity to human Dectin-1 was measured by biosensor (Octet). Single point off rate fits (k off) were determined for each clone and compared to the parental clone (delta), as shown in **FIG. 71**. Binding data are shown in Table 9. Notable changes to binding properties are bolded. CDR sequences for selected 2M24 variant clones (2M24.1.14, 2M24.1.15, 2M24.1.20, 2M24.1.24, and 2M24.1.26) are shown in Table 10.

Table 9. Biosensor binding data for alanine variants of 2M24.

Clone	**X=340**	**X=470**	**delta**	**k off**
2M24.1.25	0.475	0.432	9%	7.79E-04
2M24.1.26	**0.231**	**0.018**	**92%**	**5.41E-02**
2M24.1.27	0.483	0.393	19%	1.93E-03
2M24.1.28	**0.309**	**0.031**	**90%**	**3.56E-02**
2M24.1.29	0.456	0.350	23%	2.52E-03
Parent	0.442	0.383	13%	1.35E-03
2M24.1.1	**0.305**	**0.006**	**98%**	**2.81E-02**
2M24.1.2	**0.331**	**0.006**	**98%**	**3.07E-02**
2M24.1.3	0.000	0.000		
2M24.1.4	0.000	0.000		
2M24.1.5	**0.300**	**0.014**	**95%**	**2.50E-02**
2M24.1.6	0.493	0.390	21%	2.12E-03
2M24.1.7	0.510	0.398	22%	2.29E-03
Parent	0.499	0.428	14%	1.39E-03
2M24.1.8	**0.042**	**0.000**	**100%**	**5.44E-01**
2M24.1.9	**0.018**	**0.000**	**100%**	**1.20E+00**
2M24.1.10	0.490	0.402	18%	1.96E-03
2M24.1.11	0.499	0.418	16%	1.65E-03
2M24.1.12	0.490	0.399	19%	1.89E-03
2M24.1.14	**0.106**	**0.000**	**100%**	**3.13E-01**
2M24.1.13	**0.028**	**0.000**	**100%**	**8.09E-01**
Parent	0.508	0.435	14%	1.39E-03
Clone	**X=290**	**X=350**	**delta**	**K off**
2M24.1.15	**0.0820**	**0.0314**	**62%**	**2.39E-02**
2M24.1.16	0.1198	0.1140	5%	1.61E-03

2M24.1.17	0.1305	0.1294	1%	6.45E-04
2M24.1.18	0.1375	0.1245	9%	1.92E-03
2M24.1.19	0.1259	0.0983	22%	5.94E-03
2M24.1.20	**0.0981**	**0.0215**	**78%**	**3.60E-02**
2M24.1.21	0.1247	0.1142	8%	2.38E-03
2M24.1.22	0.1309	0.1119	15%	3.32E-03
2M24.1.23	0.1280	0.1044	18%	5.36E-03
2M24.1.24	**0.1146**	**0.0730**	**36%**	**1.05E-02**
Parent	0.1287	0.1231	4%	1.20E-03

Table 10. CDR sequences for 2M24 alanine variant clones.

Name	*CDR-H1*	*CDR-H2*	*CDR-H3*	*CDR-L1*	*CDR-L2*	*CDR-L3*
2M24 (Kabat)	DYYI (SEQ ID NO: 1)	WINPNSGDTNYAQKFQG (SEQ ID NO: 2)	NSGSYSFGY (SEQ ID NO: 3)	RASQGISSWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYSFPFT (SEQ ID NO: 6)
2M24 (IMGT)	GYTFTDYY (SEQ ID NO:7)	INPNSGDT (SEQ ID NO: 8)	ARNSGSYSFGY (SEQ ID NO: 9)	QGISSW (SEQ ID NO: 10)	GAS (SEQ ID NO: 11)	QQAYSFPFT (SEQ ID NO: 12)
2M24 (Chothia)	GYTFTDY (SEQ ID NO:13)	NPNSGD (SEQ ID NO: 14)	NSGSYSFGY (SEQ ID NO: 15)	RASQGISSWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYSFPFT (SEQ ID NO: 6)
2M24.1.14 (Kabat)	DYYI (SEQ ID NO: 1)	WINPNSGDTNYAQKFQG (SEQ ID NO: 2)	NSGSASFGY (SEQ ID NO: 187)	RASQGISSWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYSFPFT (SEQ ID NO: 6)
2M24.1.14 (IMGT)	GYTFTDYY (SEQ ID NO:7)	INPNSGDT (SEQ ID NO: 8)	ARNSGSASFGY (SEQ ID NO: 188)	QGISSW (SEQ ID NO: 10)	GAS (SEQ ID NO: 11)	QQAYSFPFT (SEQ ID NO: 12)
2M24.1.14 (Chothia)	GYTFTDY (SEQ ID NO:13)	NPNSGD (SEQ ID NO: 14)	NSGSASFGY (SEQ ID NO: 187)	RASQGISSWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYSFPFT (SEQ ID NO: 6)
2M24.1.15 (Kabat)	DYYI (SEQ ID NO: 1)	WINPNSGDTNYAQKFQG (SEQ ID NO: 2)	NSGSYSFGY (SEQ ID NO: 3)	RASQGISSWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYSFPFT (SEQ ID NO: 6)
2M24.1.15 (IMGT)	GYTFTDYY (SEQ ID NO:7)	INPNSGDT (SEQ ID NO: 8)	AANSGSYSFGY (SEQ ID NO: 189)	QGISSW (SEQ ID NO: 10)	GAS (SEQ ID NO: 11)	QQAYSFPFT (SEQ ID NO: 12)
2M24.1.15 (Chothia)	GYTFTDY (SEQ ID NO:13)	NPNSGD (SEQ ID NO: 14)	NSGSYSFGY (SEQ ID NO: 15)	RASQGISSWLA	GASSLQS (SEQ ID NO: 5)	QQAYSFPFT (SEQ ID NO: 6)

				(SEQ ID NO: 4)		
2M24.1.20 (Kabat)	DYYI (SEQ ID NO: 1)	WINPNSGDTNYAQKFQG (SEQ ID NO: 2)	NSGSYSAGY (SEQ ID NO: 190)	RASQGISSWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYSFPFT (SEQ ID NO: 6)
2M24.1.20 (IMGT)	GYTFTDYY (SEQ ID NO:7)	INPNSGDT (SEQ ID NO: 8)	ARNSGSYSAGY (SEQ ID NO: 191)	QGISSW (SEQ ID NO: 10)	GAS (SEQ ID NO: 11)	QQAYSFPFT (SEQ ID NO: 12)
2M24.1.20 (Chothia)	GYTFTDY (SEQ ID NO:13)	NPNSGD (SEQ ID NO: 14)	NSGSYSAGY (SEQ ID NO: 190)	RASQGISSWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYSFPFT (SEQ ID NO: 6)
2M24.1.24 (Kabat)	DYYI (SEQ ID NO: 1)	WINPNSGDTNYAQKFQG (SEQ ID NO: 2)	NSGSYSFGY (SEQ ID NO: 3)	RASQGISSWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QAAYSFPFT (SEQ ID NO: 192)
2M24.1.24 (IMGT)	GYTFTDYY (SEQ ID NO:7)	INPNSGDT (SEQ ID NO: 8)	ARNSGSYSFGY (SEQ ID NO: 9)	QGISSW (SEQ ID NO: 10)	GAS (SEQ ID NO: 11)	QAAYSFPFT (SEQ ID NO: 192)
2M24.1.24 (Chothia)	GYTFTDY (SEQ ID NO:13)	NPNSGD (SEQ ID NO: 14)	NSGSYSFGY (SEQ ID NO: 15)	RASQGISSWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QAAYSFPFT (SEQ ID NO: 192)
2M24.1.26 (Kabat)	DYYI (SEQ ID NO: 1)	WINPNSGDTNYAQKFQG (SEQ ID NO: 2)	NSGSYSFGY (SEQ ID NO: 3)	RASQGISSWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYSAPFT (SEQ ID NO: 193)
2M24.1.26 (IMGT)	GYTFTDYY (SEQ ID NO:7)	INPNSGDT (SEQ ID NO: 8)	ARNSGSYSFGY (SEQ ID NO: 9)	QGISSW (SEQ ID NO: 10)	GAS (SEQ ID NO: 11)	QQAYSAPFT (SEQ ID NO: 193)
2M24.1.26 (Chothia)	GYTFTDY (SEQ ID NO:13)	NPNSGD (SEQ ID NO: 14)	NSGSYSFGY (SEQ ID NO: 15)	RASQGISSWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYSAPFT (SEQ ID NO: 193)

[0379] These results demonstrate the importance of certain CDR residues for binding affinity of 2M24 variants to human Dectin-1 and provide variant anti-Dectin-1 variable domains with a gradient in binding affinity to human Dectin-1.

Example 18: Generating variant binding domains that bind human Dectin-1 to remove potential liabilities

[0380] This Example describes the introduction of substitutions at specific positions in the 2M24 variable domains in order to remove potential liabilities, *e.g.*, potential manufacturing issues (*e.g.*, chemical liabilities), and to decrease the potential risk of immunogenicity. The goal of these experiments

is to replace residues that represent potential liabilities with residues having decreased liability risk while maintaining binding affinity to human Dectin-1.

[0381] 2M24 variable domain sequences were analyzed *in silico*, and specific residues that could represent potential liabilities were flagged. These residues were then mutated back to germline sequence. Multiple rounds of these analyses were undertaken, and 89 clones were tested in total. CDR sequences for selected 2M24 variant clones (2M24.116 and 2M24.119) are shown in Table 11.

Table 11. CDR sequences for 2M24 liability variant clones.

Name	*CDR-H1*	*CDR-H2*	*CDR-H3*	*CDR-L1*	*CDR-L2*	*CDR-L3*
2M24 (Kabat)	DYYI (SEQ ID NO: 1)	WINPNSG DTNYAQ KFQG (SEQ ID NO: 2)	NSGSYSFG Y (SEQ ID NO: 3)	RASQGIS SWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYSFPFT (SEQ ID NO: 6)
2M24 (IMGT)	GYTFTDY Y (SEQ ID NO:7)	INPNSGD T (SEQ ID NO: 8)	ARNSGSYS FGY (SEQ ID NO: 9)	QGISSW (SEQ ID NO: 10)	GAS (SEQ ID NO: 11)	QQAYSFPFT (SEQ ID NO: 12)
2M24 (Chothia)	GYTFTDY (SEQ ID NO:13)	NPNSGD (SEQ ID NO: 14)	NSGSYSFG Y (SEQ ID NO: 15)	RASQGIS SWLA (SEQ ID NO: 4)	GASSLQS (SEQ ID NO: 5)	QQAYSFPFT (SEQ ID NO: 6)
2M24.119 (Kabat)	DYYM (SEQ ID NO: 199)	WINPNEG DTNYAQ KFEG (SEQ ID NO: 200)	NTGAYSFG Y (SEQ ID NO: 204)	RASQGIS SWLA (SEQ ID NO: 4)	GASDLQS (SEQ ID NO: 206)	QQAYGFPFT (SEQ ID NO: 207)
2M24.119 (IMGT)	GYTFTDY Y (SEQ ID NO:7)	INPNEGD T (SEQ ID NO: 202)	ARNTGAYS FGY (SEQ ID NO: 205)	QGISSW (SEQ ID NO: 10)	GAS (SEQ ID NO: 11)	QQAYGFPFT (SEQ ID NO: 207)
2M24.119 (Chothia)	GYTFTDY (SEQ ID NO:13)	NPNEGD (SEQ ID NO: 203)	NTGAYSFG Y (SEQ ID NO: 204)	RASQGIS SWLA (SEQ ID NO: 4)	GASDLQS (SEQ ID NO: 206)	QQAYGFPFT (SEQ ID NO: 207)
2M24.116 (Kabat)	DYYM (SEQ ID NO: 199)	WINPNEG DTNYAQ KFQE (SEQ ID NO: 201)	NTGAYSFG Y (SEQ ID NO: 204)	RASQGIS SWLA (SEQ ID NO: 4)	GASDLQS (SEQ ID NO: 206)	HQAYSFPFT (SEQ ID NO: 208)
2M24.116 (IMGT)	GYTFTDY Y (SEQ ID NO:7)	INPNEGD T (SEQ ID NO: 202)	ARNTGAYS FGY (SEQ ID NO: 205)	QGISSW (SEQ ID NO: 10)	GAS (SEQ ID NO: 11)	HQAYSFPFT (SEQ ID NO: 208)
2M24.116 (Chothia)	GYTFTDY (SEQ ID NO:13)	NPNEGD (SEQ ID NO: 203)	NTGAYSFG Y (SEQ ID NO: 204)	RASQGIS SWLA (SEQ ID NO: 4)	GASDLQS (SEQ ID NO: 206)	HQAYSFPFT (SEQ ID NO: 208)

[0382] Potency of 2M24 variants were compared to 2M24 parental binding domains in a bispecific antibody format with an anti-Trop2 arm. Co-cultures of Trop2-expressing cells and the Dectin-1-expressing HEK reporter cells were treated with increasing concentration of 2M24/Trop2 hIgG1 bispecific antibodies or 2M24 monospecific antibodies, using 75,000 Dectin-1-expressing HEK reporter cells and 25,000 target cells (3:1 effector:target ratio) in RPMI incubated overnight at 37°C. Reporter activation was assessed by measuring SEAP levels (based on absorbance at 630 nm) in media.

[0383] The results are shown in **FIG. 72A**. 2M24 variants 2M24.116 and 2M24.119 showed similar potency to that of the parental 2M24 antibody in a bispecific format. 2M24/Trop2, 2M24.116/Trop2, and 2M24.119/Trop2 bispecific antibodies showed similar binding to A431 cells expressing Trop2, as compared to parental anti-Trop2 monospecific antibody (**FIG. 72B**). 2M24.116 and 2M24.119 showed roughly the same EC50 for binding to Dectin-1-expressing HEK cells in monospecific format as 2M24, and 2M24/Trop2, 2M24.116/Trop2, and 2M24.119/Trop2 bispecific antibodies showed similar binding to Dectin-1-expressing HEK cells (**FIG. 72C**).

[0384] These results demonstrate that 2M24 variants retained potency and binding affinity to cells expressing Dectin-1 while removing potential liabilities.

Example 19: Engineering disulfide bonds in 2M24 binding domains

[0385] This Example describes the introduction of cysteine substitutions at specific positions in the 2M24 variable domains in order to introduce engineered disulfide bonds between heavy and light chains. For formats with separate heavy and light chains, additional mutations were introduced to remove cysteine residues and hence native disulfide bonds between heavy and light chain constant domains. For these formats, the goal was to drive proper pairing between heavy and light chain (*e.g.*, in a bispecific format) by creating a distinction between the pattern of disulfide bonding between the 2M24 arm and the arm binding a target of interest (with native disulfide bonding). For single chain formats, the goal was to increase stability.

[0386] **FIG. 73** shows a traditional bispecific antibody format and a format in the arm binding Dectin-1 (using 2M24 variable domains) is in scFv format. Heavy chains are paired with knobs-into-holes mutations. In the Dectin-1 binding arms, cysteines forming native disulfide bonds between heavy and light chains have been removed, and cysteine substitutions have been introduced to give rise to non-native disulfide bonds. The arms binding the target of interest have native disulfide bonds, thereby distinguishing the variable domains for each arm by disulfide bonding position.

[0387] In order to determine suitable sites for cysteine residues to form disulfide bonds, the structure of 2M24 was modeled based on germline sequences (1-2*02 for VH and 1-12*01 for VK). The closest structure in PDB was 6XLQ, representing the CTX-2026 antibody that binds BTN3A1. CTX-2026 variable domain sequences are shown below.

CTX-2026 VH

QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMHWVRQAPGQGLEWMGWINPNSG GTKYAQKFQGRVTMTRDTSISTAYMELSRLRSDDTAVYYCARRHSDMIGYYYGMDVW GQGTTVTVSS (SEQ ID NO:217)

CTX-2026 VL

DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIYAASSLQSGVPS RFSGSGSGTDFTLTISSLQPEDFATYYCQQATDFPPTFGGGTKVEIK (SEQ ID NO:218)

[0388] Using the 6XLQ as a structural model for analyzing the 2M24 sequences, 2 positions were found where the distance between heavy and light chain variable domains was 5Å or less, as disulfide bonds are normally ~3.5Å in length. Position 1 (P1) was 5Å apart, and position 2 (P2) was 4Å apart.

[0389] Reciprocal cysteine substitutions were introduced in the 2M24 VH and VL domains to introduce engineered interchain disulfide bonds at P1 and P2. An alignment between 2M24 P1 and CTX-2026 showing position of these engineered disulfides and the corresponding VH and VL sequences is shown in **FIG. 74A**. An alignment between 2M24 P2 and CTX-2026 showing position of these engineered disulfides and the corresponding VH and VL sequences is shown in **FIG. 74B**.

[0390] Bispecific antibodies comprising a Dectin-1-binding arm with 2M24 P1 or P2 VH and VL domains and a CD20-binding arm were generated (using the format shown in **FIG. 73**, left) and purified using standard Protein A purification. 2M24 P1-containing bispecific purified as 100% monomer using standard protein A purification, while 2M24 P2-containing bispecific showed an aggregate peak that could be removed using size exclusion chromatography (SEC). Therefore the 2M24 P1-containing bispecific was selected for further testing.

[0391] Activity of these bispecific antibodies was tested in a SEAP secretion assay induced by Raji cells (expressing CD20) as described *supra*. Briefly, cells were pelleted and resuspended in HEK blue detection media. Raji and hDectin-1-expressing HEK blue cells were mixed at a 1:1 ratio (50k cells each), then plated at 100µL/well. Test antibodies were titrated 3X starting at 25µg/mL final concentration, incubated with cell mixture for 24hours, then absorbance at 630nm (OD_{630}) was measured. As shown in **FIG. 75A**, P1 and P2 variants were active in inducing Dectin-1 signaling.

[0392] Bispecific antibody comprising a Dectin-1-binding arm with 2M24 P1 VH and VL domains and a CD20-binding arm was also tested in a B cell depletion assay using PBMCs from 2 healthy donors. Briefly, PBMCs from two healthy donors – donors 01and 02 were treated with increasing concentrations of the indicated antibodies for 24 h, and subsequently analyzed by flow cytometry to quantify the levels of remaining live, CD19+ B cells (reported as a % of B cells in isotype control-treated PBMCs). As shown in **FIG. 75B**, bispecific antibody with the 2M24 P1 variable domains and active hIgG1 Fc region was able to deplete B cells.

[0393] Bispecific antibodies comprising either a Dectin-1-binding arm with parental 2M24 or a Dectin-1-binding arm with 2M24 P1 VH and VL domains (both in scFv format) and a CD20-binding arm from rituximab were also generated using the format shown in **FIG. 73** (right), then subjected to Protein A

purification. The results were analyzed using Agilent 1100 HPLC with a mobile phase of PBS (pH7.4) and Superdex® 200 Increase 5/150-GL SEC column using 0.45mL/min flow rate and 10μL injection. As shown in **FIG. 76A**, approximately 30-40% of parental 2M24 bispecifics were found in the oligomer peak, compared to less than 5% of 2M24 P1 bispecifics. This significant reduction in oligomerization indicates that the bispecific antibody with 2M24 arm having engineered disulfides was more stable than that using the parental 2M24 VH and VL domains.

[0394] Bispecific antibodies comprising either a Dectin-1-binding arm with parental 2M24 or a Dectin-1-binding arm with 2M24 P1 VH and VL domains (both in scFv format) and a CD20-binding arm from rituximab along with active human IgG1 Fc were tested for ability to bind HEK cells expressing hDectin-1 or Raji cells expressing CD20. As shown in **FIG. 76B**, bispecifics with 2M24 P1 variant scFv arm behaved similarly to those with parental 2M24 scFv arm with no notable difference in binding to either cell type.

[0395] These bispecific antibodies were also compared in SEAP reporter assays using Raji cells and hDectin-1-expressing HEK blue cells at 1:1 effector:target ratio. Again, bispecifics with 2M24 P1 variant scFv arm behaved similarly to those with parental 2M24 scFv arm with no notable difference in Dectin-1 activation (**FIG. 76C**).

[0396] Both bispecific antibodies were also compared in B cell depletion assays using human PBMCs from 2 healthy donors. Briefly, bispecific antibodies comprising either a Dectin-1-binding arm with parental 2M24 or a Dectin-1-binding arm with 2M24 P1 VH and VL domains (both in scFv format) and a CD20-binding arm from rituximab along with active human IgG1 Fc. PBMCs from two healthy donors – donors 01and 02 were treated with increasing concentrations of the indicated antibodies for 24 h, and subsequently analyzed by flow cytometry to quantify the levels of remaining live, CD19+ B cells (reported as a % of B cells in isotype control-treated PBMCs). As shown in **FIG. 76D**, bispecifics with 2M24 P1 variant scFv arm showed similar depletion function to those with parental 2M24 scFv arm.

[0397] Stability of bispecific antibodies comprising either a Dectin-1-binding arm with parental 2M24 or a Dectin-1-binding arm with 2M24 P1 VH and VL domains (both in scFv format) and a CD20-binding arm from rituximab was compared. Bispecific antibody with parental 2M24 scFv arm showed increased oligomer formation after 1 week, either at 5°C or 25°C (**FIG. 76E**). In contrast, bispecific antibody with 2M24 P1 variant scFv arm showed no significant increase in oligomerization even after 4 weeks at 5°C or 25°C. These results demonstrate the increased stability of the engineered disulfide variants of 2M24.

Example 20: Tuning of binding affinity of myeloid engagers

[0398] This Example describes testing variant Fc domains in order to modulate the properties of myeloid engagers of the present disclosure.

[0399] 2M24/CD20 bispecific binding proteins were generated with human IgG4, human IgG1, or non-fucosylated human IgG1 Fc regions and tested for ability to deplete B cells in healthy human PBMCs

from 2 donors. As shown in **FIG. 77**, varying levels of depletion were observed, including changes to EC50 and depth of depletion. Non-fucosylated IgG1 led to strongest depletion, and IgG4 had the weakest. These results demonstrate that properties of myeloid engagers (*e.g.*, B cell depletion for those that bind Dectin-1 and CD20) can be tuned to various degrees using different Fc regions.

[0400] Although the present disclosure has been described in some detail by way of illustration and example for purposes of clarity of understanding, the descriptions and examples should not be construed as limiting the scope of the present disclosure. The disclosures of all patent and scientific literature cited herein are expressly incorporated in the entirety by reference.

CLAIMS

What is claimed is:

1. An antibody or antigen-binding fragment thereof that binds to human Dectin-1, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain;

wherein the VH domain comprises the amino acid sequence QVQLVQSGAEVKKPGASVKVSCKSSGYTFTX$_1$YYIHWVRQAPGQGLEWMGWINPNSGX$_2$TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCAX$_3$X$_4$X$_5$X$_6$X$_7$X$_8$X$_9$X$_{10}$X$_{11}$X$_{12}$WGQGTLVTVSS, wherein X$_1$ is D, A, or G; wherein X$_2$ is D, A, or G; wherein X$_3$ is R, A, or G; wherein X$_4$ is N, A, or G; wherein X$_5$ is S, A, or G; wherein X$_6$ is A or G; wherein X$_7$ is S, A, or G; wherein X$_8$ is Y, A, or G; wherein X$_9$ is S, A, or G; wherein X$_{10}$ is F, A, or G; wherein X$_{11}$ is A or G; and wherein X$_{12}$ is Y, A, or G (SEQ ID NO:63); and

wherein the VL domain comprises the amino acid sequence DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPSRFSGSGSGTDFTLTVSSLQPEDFATYYCX$_1$X$_2$AX$_3$X$_4$X$_5$X$_6$X$_7$X$_8$FGPGTKVDIE, wherein X$_1$ is Q, A, or G; X$_2$ is Q, A, or G; X$_3$ is F, Y, A, or G; wherein X$_4$ is S, A, or G; wherein X$_5$ is F, A, or G; wherein X$_6$ is P, A, or G; wherein X$_7$ is F, A, or G; and wherein X$_8$ is T, A, or G (SEQ ID NO:65).

2. The antibody of claim 1, wherein the antibody does not comprise a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3), a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6)

3. The antibody of claim 1 or claim 2, wherein the VH domain comprises 1, 2 or fewer, 3 or fewer, 4 or fewer, or 5 or fewer substitutions as compared to the amino acid sequence of SEQ ID NO:62; and/or wherein the VL domain comprises 1, 2 or fewer, 3 or fewer, 4 or fewer, or 5 or fewer substitutions as compared to the amino acid sequence of SEQ ID NO:64.

4. The antibody of any one of claims 1-3, wherein the antibody or fragment:

(a) binds to human Dectin-1 expressed on the surface of a cell with an EC50 of less than 2nM;

(b) is capable of binding human or cynomolgus Dectin-1; and/or

(c) does not compete with a native ligand of human Dectin-1.

5. An antibody or antigen-binding fragment thereof that binds to human Dectin-1, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain;

wherein the VH domain comprises: a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1) or AYYI (SEQ ID NO: 16); a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2) or WINPNSGATNYAQKFQG (SEQ ID NO: 19); and a CDR-H3 comprising an amino acid sequence selected from the group consisting of NSGSYSFGY (SEQ ID NO: 3), ASGSYSFGY (SEQ ID NO: 22), NSGSASFGY (SEQ ID NO: 24), NAGSYSFGY (SEQ ID NO: 27), NSASYSFGY (SEQ ID NO: 29), NSGAYSFGY (SEQ ID NO: 31), NSGSYAFGY (SEQ ID NO: 33), NSGSYSAGY (SEQ ID NO: 35), NSGSYSFAY (SEQ ID NO: 37), and NSGSYSFGA (SEQ ID NO: 39); and

wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4); a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising an amino acid sequence selected from the group consisting of QQAYSFPFT (SEQ ID NO: 6), QQAASFPFT (SEQ ID NO: 41), QQAFSFPFT (SEQ ID NO: 42), AQAYSFPFT (SEQ ID NO: 43), QAAYSFPFT (SEQ ID NO: 44), QQAYAFPFT (SEQ ID NO: 45), QQAYSAPFT (SEQ ID NO: 46), QQAYSFAFT (SEQ ID NO: 47), QQAYSFPAT (SEQ ID NO: 48), and QQAYSFPFA (SEQ ID NO: 49).

6. The antibody of claim 5, wherein the antibody does not comprise a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3), a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6).

7. The antibody of any one of claims 1-6, wherein the VH domain comprises:

(a) a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3);

(b) a CDR-H1 comprising the amino acid sequence AYYI (SEQ ID NO: 16), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3);

(c) a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGATNYAQKFQG (SEQ ID NO: 19), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3);

(d) a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence ASGSYSFGY (SEQ ID NO: 22);

(e) a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSASFGY (SEQ ID NO: 24);

(f) a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NAGSYSFGY (SEQ ID NO: 27);

(g) a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSASYSFGY (SEQ ID NO: 29);

(h) a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGAYSFGY (SEQ ID NO: 31);

(i) a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYAFGY (SEQ ID NO: 33);

(j) a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSAGY (SEQ ID NO: 35);

(k) a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSFAY (SEQ ID NO: 37); or

(l) a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSFGA (SEQ ID NO: 39).

8. The antibody of any one of claims 1-7, wherein the VH domain further comprises:

(a) a FR1 comprising an amino acid sequence selected from the group consisting of QVQLVQSGAEVKKPGASVKVSCKSSGYTFT (SEQ ID NO:50) and QVQLVQSGAEVKKPGASVKVSCKASGYTFT (SEQ ID NO:51);

(b) a FR2 comprising the amino acid sequence HWVRQAPGQGLEWMG (SEQ ID NO:52);

(c) a FR3 comprising an amino acid sequence selected from the group consisting of RITMTRDTSISTAYLELSRLRSDDTAVFYCAR (SEQ ID NO:53) and RVTMTRDTSISTAYMELSRLRSDDTAVYYCAR (SEQ ID NO:54); and

(d) a FR4 comprising the amino acid sequence WGQGTLVTVSS (SEQ ID NO:55).

9. The antibody of any one of claims 1-8, wherein the VH domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos:62 and 82-93.

10. The antibody of any one of claims 1-9, wherein the VL domain comprises:

(a) a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6);

(b) a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAASFPFT (SEQ ID NO: 41);

(c) a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAFSFPFT (SEQ ID NO: 42);

(d) a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence AQAYSFPFT (SEQ ID NO: 43);

(e) a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QAAYSFPFT (SEQ ID NO: 44);

(f) a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYAFPFT (SEQ ID NO: 45);

(g) a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSAPFT (SEQ ID NO: 46);

(h) a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFAFT (SEQ ID NO: 47);

(i) a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPAT (SEQ ID NO: 48); or

(j) a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFA (SEQ ID NO: 49).

11. The antibody of any one of claims 1-10, wherein the VL domain further comprises:

(a) a FR1 comprising the amino acid sequence DIQMTQSPSSVSASVGDRVTITC (SEQ ID NO:56);

(b) a FR2 comprising an amino acid sequence selected from the group consisting of WYQQKPGKAPKLLIF (SEQ ID NO:57) and WYQQKPGKAPKLLIY (SEQ ID NO:58);

(c) a FR3 comprising an amino acid sequence selected from the group consisting of GVPSRFSGSGSGTDFTLTVSSLQPEDFATYYC (SEQ ID NO:59) and GVPSRFSGSGSGTDFTLTISSLQPEDFATYYC (SEQ ID NO:60); and

(d) a FR4 comprising the amino acid sequence FGPGTKVDIE (SEQ ID NO:61).

12. The antibody of any one of claims 1-11, wherein the VL domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos: 64 and 94-102.

13. The antibody of any one of claims 1-6, wherein:

(1) the VH domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain comprises the amino acid sequence of SEQ ID NO:94;

(2) the VH domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain comprises the amino acid sequence of SEQ ID NO:95;

(3) the VH domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain comprises the amino acid sequence of SEQ ID NO:96;

(4) the VH domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain comprises the amino acid sequence of SEQ ID NO:97;

(5) the VH domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain comprises the amino acid sequence of SEQ ID NO:98;

(6) the VH domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain comprises the amino acid sequence of SEQ ID NO:99;

(7) the VH domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain comprises the amino acid sequence of SEQ ID NO:100;

(8) the VH domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain comprises the amino acid sequence of SEQ ID NO:101;

(9) the VH domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain comprises the amino acid sequence of SEQ ID NO:102;

(10) the VH domain comprises the amino acid sequence of SEQ ID NO:82, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(11) the VH domain comprises the amino acid sequence of SEQ ID NO:82, and the VL domain comprises the amino acid sequence of SEQ ID NO:94;

(12) the VH domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain comprises the amino acid sequence of SEQ ID NO:95;

(13) the VH domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain comprises the amino acid sequence of SEQ ID NO:96;

(14) the VH domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain comprises the amino acid sequence of SEQ ID NO:97;

(15) the VH domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain comprises the amino acid sequence of SEQ ID NO:98;

(16) the VH domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain comprises the amino acid sequence of SEQ ID NO:99;

(17) the VH domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain comprises the amino acid sequence of SEQ ID NO:100;

(18) the VH domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain comprises the amino acid sequence of SEQ ID NO:101;

(19) the VH domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain comprises the amino acid sequence of SEQ ID NO:102;

(20) the VH domain comprises the amino acid sequence of SEQ ID NO:83, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(21) the VH domain comprises the amino acid sequence of SEQ ID NO:83, and the VL domain comprises the amino acid sequence of SEQ ID NO:94;

(22) the VH domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain comprises the amino acid sequence of SEQ ID NO:95;

(23) the VH domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain comprises the amino acid sequence of SEQ ID NO:96;

(24) the VH domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain comprises the amino acid sequence of SEQ ID NO:97;

(25) the VH domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain comprises the amino acid sequence of SEQ ID NO:98;

(26) the VH domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain comprises the amino acid sequence of SEQ ID NO:99;

(27) the VH domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain comprises the amino acid sequence of SEQ ID NO:100;

(28) the VH domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain comprises the amino acid sequence of SEQ ID NO:101;

(29) the VH domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain comprises the amino acid sequence of SEQ ID NO:102;

(30) the VH domain comprises the amino acid sequence of SEQ ID NO:84, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(31) the VH domain comprises the amino acid sequence of SEQ ID NO:84, and the VL domain comprises the amino acid sequence of SEQ ID NO:94;

(32) the VH domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain comprises the amino acid sequence of SEQ ID NO:95;

(33) the VH domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain comprises the amino acid sequence of SEQ ID NO:96;

(34) the VH domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain comprises the amino acid sequence of SEQ ID NO:97;

(35) the VH domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain comprises the amino acid sequence of SEQ ID NO:98;

(36) the VH domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain comprises the amino acid sequence of SEQ ID NO:99;

(37) the VH domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain comprises the amino acid sequence of SEQ ID NO:100;

(38) the VH domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain comprises the amino acid sequence of SEQ ID NO:101;

(39) the VH domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain comprises the amino acid sequence of SEQ ID NO:102;

(40) the VH domain comprises the amino acid sequence of SEQ ID NO:85, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(41) the VH domain comprises the amino acid sequence of SEQ ID NO:85, and the VL domain comprises the amino acid sequence of SEQ ID NO:94;

(42) the VH domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain comprises the amino acid sequence of SEQ ID NO:95;

(43) the VH domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain comprises the amino acid sequence of SEQ ID NO:96;

(44) the VH domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain comprises the amino acid sequence of SEQ ID NO:97;

(45) the VH domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain comprises the amino acid sequence of SEQ ID NO:98;

(46) the VH domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain comprises the amino acid sequence of SEQ ID NO:99;

(47) the VH domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain comprises the amino acid sequence of SEQ ID NO:100;

(48) the VH domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain comprises the amino acid sequence of SEQ ID NO:101;

(49) the VH domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain comprises the amino acid sequence of SEQ ID NO:102;

(50) the VH domain comprises the amino acid sequence of SEQ ID NO:86, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(51) the VH domain comprises the amino acid sequence of SEQ ID NO:86, and the VL domain comprises the amino acid sequence of SEQ ID NO:94;

(52) the VH domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain comprises the amino acid sequence of SEQ ID NO:95;

(53) the VH domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain comprises the amino acid sequence of SEQ ID NO:96;

(54) the VH domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain comprises the amino acid sequence of SEQ ID NO:97;

(55) the VH domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain comprises the amino acid sequence of SEQ ID NO:98;

(56) the VH domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain comprises the amino acid sequence of SEQ ID NO:99;

(57) the VH domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain comprises the amino acid sequence of SEQ ID NO:100;

(58) the VH domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain comprises the amino acid sequence of SEQ ID NO:101;

(59) the VH domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain comprises the amino acid sequence of SEQ ID NO:102;

(60) the VH domain comprises the amino acid sequence of SEQ ID NO:87, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(61) the VH domain comprises the amino acid sequence of SEQ ID NO:87, and the VL domain comprises the amino acid sequence of SEQ ID NO:94;

(62) the VH domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain comprises the amino acid sequence of SEQ ID NO:95;

(63) the VH domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain comprises the amino acid sequence of SEQ ID NO:96;

(64) the VH domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain comprises the amino acid sequence of SEQ ID NO:97;

(65) the VH domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain comprises the amino acid sequence of SEQ ID NO:98;

(66) the VH domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain comprises the amino acid sequence of SEQ ID NO:99;

(67) the VH domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain comprises the amino acid sequence of SEQ ID NO:100;

(68) the VH domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain comprises the amino acid sequence of SEQ ID NO:101;

(69) the VH domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain comprises the amino acid sequence of SEQ ID NO:102;

(70) the VH domain comprises the amino acid sequence of SEQ ID NO:88, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(71) the VH domain comprises the amino acid sequence of SEQ ID NO:88, and the VL domain comprises the amino acid sequence of SEQ ID NO:94;

(72) the VH domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain comprises the amino acid sequence of SEQ ID NO:95;

(73) the VH domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain comprises the amino acid sequence of SEQ ID NO:96;

(74) the VH domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain comprises the amino acid sequence of SEQ ID NO:97;

(75) the VH domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain comprises the amino acid sequence of SEQ ID NO:98;

(76) the VH domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain comprises the amino acid sequence of SEQ ID NO:99;

(77) the VH domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain comprises the amino acid sequence of SEQ ID NO:100;

(78) the VH domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain comprises the amino acid sequence of SEQ ID NO:101;

(79) the VH domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain comprises the amino acid sequence of SEQ ID NO:102;

(80) the VH domain comprises the amino acid sequence of SEQ ID NO:89, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(81) the VH domain comprises the amino acid sequence of SEQ ID NO:89, and the VL domain comprises the amino acid sequence of SEQ ID NO:94;

(82) the VH domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain comprises the amino acid sequence of SEQ ID NO:95;

(83) the VH domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain comprises the amino acid sequence of SEQ ID NO:96;

(84) the VH domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain comprises the amino acid sequence of SEQ ID NO:97;

(85) the VH domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain comprises the amino acid sequence of SEQ ID NO:98;

(86) the VH domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain comprises the amino acid sequence of SEQ ID NO:99;

(87) the VH domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain comprises the amino acid sequence of SEQ ID NO:100;

(88) the VH domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain comprises the amino acid sequence of SEQ ID NO:101;

(89) the VH domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain comprises the amino acid sequence of SEQ ID NO:102;

(90) the VH domain comprises the amino acid sequence of SEQ ID NO:90, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(91) the VH domain comprises the amino acid sequence of SEQ ID NO:90, and the VL domain comprises the amino acid sequence of SEQ ID NO:94;

(92) the VH domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain comprises the amino acid sequence of SEQ ID NO:95;

(93) the VH domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain comprises the amino acid sequence of SEQ ID NO:96;

(94) the VH domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain comprises the amino acid sequence of SEQ ID NO:97;

(95) the VH domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain comprises the amino acid sequence of SEQ ID NO:98;

(96) the VH domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain comprises the amino acid sequence of SEQ ID NO:99;

(97) the VH domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain comprises the amino acid sequence of SEQ ID NO:100;

(98) the VH domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain comprises the amino acid sequence of SEQ ID NO:101;

(99) the VH domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain comprises the amino acid sequence of SEQ ID NO:102;

(100) the VH domain comprises the amino acid sequence of SEQ ID NO:91, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(101) the VH domain comprises the amino acid sequence of SEQ ID NO:91, and the VL domain comprises the amino acid sequence of SEQ ID NO:94;

(102) the VH domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain comprises the amino acid sequence of SEQ ID NO:95;

(103) the VH domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain comprises the amino acid sequence of SEQ ID NO:96;

(104) the VH domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain comprises the amino acid sequence of SEQ ID NO:97;

(105) the VH domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain comprises the amino acid sequence of SEQ ID NO:98;

(106) the VH domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain comprises the amino acid sequence of SEQ ID NO:99;

(107) the VH domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain comprises the amino acid sequence of SEQ ID NO:100;

(108) the VH domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain comprises the amino acid sequence of SEQ ID NO:101;

(109) the VH domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain comprises the amino acid sequence of SEQ ID NO:102;

(110) the VH domain comprises the amino acid sequence of SEQ ID NO:92, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(111) the VH domain comprises the amino acid sequence of SEQ ID NO:92, and the VL domain comprises the amino acid sequence of SEQ ID NO:94;

(112) the VH domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain comprises the amino acid sequence of SEQ ID NO:95;

(113) the VH domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain comprises the amino acid sequence of SEQ ID NO:96;

(114) the VH domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain comprises the amino acid sequence of SEQ ID NO:97;

(115) the VH domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain comprises the amino acid sequence of SEQ ID NO:98;

(116) the VH domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain comprises the amino acid sequence of SEQ ID NO:99;

(117) the VH domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain comprises the amino acid sequence of SEQ ID NO:100;

(118) the VH domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain comprises the amino acid sequence of SEQ ID NO:101;

(119) the VH domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain comprises the amino acid sequence of SEQ ID NO:102;

(120) the VH domain comprises the amino acid sequence of SEQ ID NO:93, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(121) the VH domain comprises the amino acid sequence of SEQ ID NO:93, and the VL domain comprises the amino acid sequence of SEQ ID NO:94;

(122) the VH domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain comprises the amino acid sequence of SEQ ID NO:95;

(123) the VH domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain comprises the amino acid sequence of SEQ ID NO:96;

(124) the VH domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain comprises the amino acid sequence of SEQ ID NO:97;

(125) the VH domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain comprises the amino acid sequence of SEQ ID NO:98;

(126) the VH domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain comprises the amino acid sequence of SEQ ID NO:99;

(127) the VH domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain comprises the amino acid sequence of SEQ ID NO:100;

(128) the VH domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain comprises the amino acid sequence of SEQ ID NO:101; or

(129) the VH domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain comprises the amino acid sequence of SEQ ID NO:102.

14. An antibody or antigen-binding fragment thereof that binds to human Dectin-1, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain;

wherein the VH domain comprises the amino acid sequence QVQLVQSGAEVKKPGASVKVSCKX$_1$SGYTFTX$_2$YYX$_3$HWVRQAPGQGLEWMGWINPNSGX$_4$TNYAQKFQGRX$_5$TMTRDTSISTAYX$_6$ELSRLRSDDTAVX$_7$YCARNSGSYSFGYWGQGTLVTVSS; wherein X$_1$ is S or A; wherein X$_2$ is D or G; wherein X$_3$ is I or M; wherein X$_4$ is D or G; wherein X$_5$ is I or V; wherein X$_6$ is L or M; and wherein X$_7$ is F or Y (SEQ ID NO:80); and

wherein the VL domain comprises the amino acid sequence DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIX$_1$X$_2$ASSLQSGVPSRFSGSGSGTDFTLTX$_3$SSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE; wherein X$_1$ is F or Y; wherein X$_2$ is G or A; and wherein X$_3$ is V or I (SEQ ID NO:81).

15. An antibody or antigen-binding fragment thereof that binds to human Dectin-1, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain;

wherein the VH domain comprises: a CDR-H1 comprising an amino acid sequence selected from the group consisting of DYYI (SEQ ID NO: 1), DYYM (SEQ ID NO: 66), and GYYM (SEQ ID NO: 67); a CDR-H2 comprising the amino acid sequence

WINPNSGDTNYAQKFQG (SEQ ID NO: 2) or WINPNSGGTNYAQKFQG (SEQ ID NO: 70); and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3); and

wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4); a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5) or AASSLQS (SEQ ID NO: 73), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6).

16. The antibody of claim 14 or claim 15, wherein the antibody does not comprise a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3), a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6).

17. The antibody of any one of claims 14-16, wherein the VH domain comprises:

(a) a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3);

(b) a CDR-H1 comprising the amino acid sequence DYYM (SEQ ID NO: 66), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3);

(c) a CDR-H1 comprising the amino acid sequence GYYM (SEQ ID NO: 67), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3);

(d) a CDR-H1 comprising the amino acid sequence DYYM (SEQ ID NO: 66), a CDR-H2 comprising the amino acid sequence WINPNSGGTNYAQKFQG (SEQ ID NO: 70), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3); or

(e) a CDR-H1 comprising the amino acid sequence GYYM (SEQ ID NO: 67), a CDR-H2 comprising the amino acid sequence WINPNSGGTNYAQKFQG (SEQ ID NO: 70), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3).

18. The antibody of any one of claims 14-17, wherein the VH domain further comprises:

(a) a FR1 comprising an amino acid sequence selected from the group consisting of QVQLVQSGAEVKKPGASVKVSCKSSGYTFT (SEQ ID NO:50) and QVQLVQSGAEVKKPGASVKVSCKASGYTFT (SEQ ID NO:76);

(b) a FR2 comprising the amino acid sequence HWVRQAPGQGLEWMG (SEQ ID NO:52);

(c) a FR3 comprising an amino acid sequence selected from the group consisting of RITMTRDTSISTAYLELSRLRSDDTAVFYCAR (SEQ ID NO:53) and RVTMTRDTSISTAYMELSRLRSDDTAVYYCAR (SEQ ID NO:77); and

(d) a FR4 comprising the amino acid sequence WGQGTLVTVSS (SEQ ID NO:55).

19. The antibody of any one of claims 14-18, wherein the VH domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos: 62 and 103-109.

20. The antibody of any one of claims 14-19, wherein the VL domain comprises:

(a) a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6); or

(b) a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence AASSLQS (SEQ ID NO: 73), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6).

21. The antibody of any one of claims 14-20, wherein the VL domain further comprises:

(a) a FR1 comprising the amino acid sequence DIQMTQSPSSVSASVGDRVTITC (SEQ ID NO:56);

(b) a FR2 comprising an amino acid sequence selected from the group consisting of WYQQKPGKAPKLLIF (SEQ ID NO:57) and WYQQKPGKAPKLLIY (SEQ ID NO:78);

(c) a FR3 comprising an amino acid sequence selected from the group consisting of GVPSRFSGSGSGTDFTLTVSSLQPEDFATYYC (SEQ ID NO:59) and GVPSRFSGSGSGTDFTLTISSLQPEDFATYYC (SEQ ID NO:79); and

(d) a FR4 comprising the amino acid sequence FGPGTKVDIE (SEQ ID NO:61).

22. The antibody of any one of claims 14-21, wherein the VL domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos:64 and 110-113.

23. The antibody of any one of claims 14-16, wherein:

(1) the VH domain comprises the amino acid sequence of SEQ ID NO: 62, and the VL domain comprises the amino acid sequence of SEQ ID NO:110;

(2) the VH domain comprises the amino acid sequence of SEQ ID NO: 62, and the VL domain comprises the amino acid sequence of SEQ ID NO:111;

(3) the VH domain comprises the amino acid sequence of SEQ ID NO: 62, and the VL domain comprises the amino acid sequence of SEQ ID NO:112;

(4) the VH domain comprises the amino acid sequence of SEQ ID NO: 62, and the VL domain comprises the amino acid sequence of SEQ ID NO:113;

(5) the VH domain comprises the amino acid sequence of SEQ ID NO: 103, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(6) the VH domain comprises the amino acid sequence of SEQ ID NO: 103, and the VL domain comprises the amino acid sequence of SEQ ID NO:110;

(7) the VH domain comprises the amino acid sequence of SEQ ID NO: 103, and the VL domain comprises the amino acid sequence of SEQ ID NO:111;

(8) the VH domain comprises the amino acid sequence of SEQ ID NO: 103, and the VL domain comprises the amino acid sequence of SEQ ID NO:112;

(9) the VH domain comprises the amino acid sequence of SEQ ID NO: 103, and the VL domain comprises the amino acid sequence of SEQ ID NO:113;

(10) the VH domain comprises the amino acid sequence of SEQ ID NO: 104, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(11) the VH domain comprises the amino acid sequence of SEQ ID NO: 104, and the VL domain comprises the amino acid sequence of SEQ ID NO:110;

(12) the VH domain comprises the amino acid sequence of SEQ ID NO: 104, and the VL domain comprises the amino acid sequence of SEQ ID NO:111;

(13) the VH domain comprises the amino acid sequence of SEQ ID NO: 104, and the VL domain comprises the amino acid sequence of SEQ ID NO:112;

(14) the VH domain comprises the amino acid sequence of SEQ ID NO: 104, and the VL domain comprises the amino acid sequence of SEQ ID NO:113;

(15) the VH domain comprises the amino acid sequence of SEQ ID NO: 105, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(16) the VH domain comprises the amino acid sequence of SEQ ID NO: 105, and the VL domain comprises the amino acid sequence of SEQ ID NO:110;

(17) the VH domain comprises the amino acid sequence of SEQ ID NO: 105, and the VL domain comprises the amino acid sequence of SEQ ID NO:111;

(18) the VH domain comprises the amino acid sequence of SEQ ID NO: 105, and the VL domain comprises the amino acid sequence of SEQ ID NO:112;

(19) the VH domain comprises the amino acid sequence of SEQ ID NO: 105, and the VL domain comprises the amino acid sequence of SEQ ID NO:113;

(20) the VH domain comprises the amino acid sequence of SEQ ID NO: 106, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(21) the VH domain comprises the amino acid sequence of SEQ ID NO: 106, and the VL domain comprises the amino acid sequence of SEQ ID NO:110;

(22) the VH domain comprises the amino acid sequence of SEQ ID NO: 106, and the VL domain comprises the amino acid sequence of SEQ ID NO:111;

(23) the VH domain comprises the amino acid sequence of SEQ ID NO: 106, and the VL domain comprises the amino acid sequence of SEQ ID NO:112;

(24) the VH domain comprises the amino acid sequence of SEQ ID NO: 106, and the VL domain comprises the amino acid sequence of SEQ ID NO:113;

(25) the VH domain comprises the amino acid sequence of SEQ ID NO: 107, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(26) the VH domain comprises the amino acid sequence of SEQ ID NO: 107, and the VL domain comprises the amino acid sequence of SEQ ID NO:110;

(27) the VH domain comprises the amino acid sequence of SEQ ID NO: 107, and the VL domain comprises the amino acid sequence of SEQ ID NO:111;

(28) the VH domain comprises the amino acid sequence of SEQ ID NO: 107, and the VL domain comprises the amino acid sequence of SEQ ID NO:112;

(29) the VH domain comprises the amino acid sequence of SEQ ID NO: 107, and the VL domain comprises the amino acid sequence of SEQ ID NO:113;

(30) the VH domain comprises the amino acid sequence of SEQ ID NO: 108, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(31) the VH domain comprises the amino acid sequence of SEQ ID NO: 108, and the VL domain comprises the amino acid sequence of SEQ ID NO:110;

(32) the VH domain comprises the amino acid sequence of SEQ ID NO: 108, and the VL domain comprises the amino acid sequence of SEQ ID NO:111;

(33) the VH domain comprises the amino acid sequence of SEQ ID NO: 108, and the VL domain comprises the amino acid sequence of SEQ ID NO:112;

(34) the VH domain comprises the amino acid sequence of SEQ ID NO: 108, and the VL domain comprises the amino acid sequence of SEQ ID NO:113;

(35) the VH domain comprises the amino acid sequence of SEQ ID NO: 109, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(36) the VH domain comprises the amino acid sequence of SEQ ID NO: 109, and the VL domain comprises the amino acid sequence of SEQ ID NO:110;

(37) the VH domain comprises the amino acid sequence of SEQ ID NO: 109, and the VL domain comprises the amino acid sequence of SEQ ID NO:111;

(38) the VH domain comprises the amino acid sequence of SEQ ID NO: 109, and the VL domain comprises the amino acid sequence of SEQ ID NO:112; or

(39) the VH domain comprises the amino acid sequence of SEQ ID NO: 109, and the VL domain comprises the amino acid sequence of SEQ ID NO:113.

24. The antibody of claim 15, wherein the VH domain comprises the amino acid sequence of SEQ ID NO: 213, and the VL domain comprises the amino acid sequence of SEQ ID NO:214.

25. The antibody of claim 15, wherein the VH domain comprises the amino acid sequence of SEQ ID NO: 195, and the VL domain comprises the amino acid sequence of SEQ ID NO:64.

26. An antibody or antigen-binding fragment thereof that binds to human Dectin-1, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain;

wherein the VH domain comprises: a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1) or DYYM (SEQ ID NO: 199); a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), WINPNEGDTNYAQKFEG (SEQ ID NO: 200), or WINPNEGDTNYAQKFQE (SEQ ID NO: 201); and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3), NSGSASFGY (SEQ ID NO: 187), NSGSYSAGY (SEQ ID NO: 190), or NTGAYSFGY (SEQ ID NO: 204); and

wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4); a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5) or GASDLQS (SEQ ID NO: 206), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6), QAAYSFPFT (SEQ ID NO: 192), QQAYSAPFT (SEQ ID NO: 193), QQAYGFPFT (SEQ ID NO: 207), or HQAYSFPFT (SEQ ID NO: 208);

wherein the antibody does not comprise a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3), a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6).

27. The antibody of claim 26, wherein:

(a) the VH domain comprises: a CDR-H1 comprising the amino acid sequence of DYYM (SEQ ID NO: 199), a CDR-H2 comprising the amino acid sequence of WINPNEGDTNYAQKFEG (SEQ ID NO: 200), and a CDR-H3 comprising the amino acid sequence of NTGAYSFGY (SEQ ID NO: 204), and the VL domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASDLQS (SEQ ID NO: 206), and a CDR-L3 comprising the amino acid sequence of QQAYGFPFT (SEQ ID NO: 207);

(b) the VH domain comprises: a CDR-H1 comprising the amino acid sequence of DYYM (SEQ ID NO: 199), a CDR-H2 comprising the amino acid sequence of WINPNEGDTNYAQKFQE (SEQ ID NO: 201), and a CDR-H3 comprising the amino acid sequence of NTGAYSFGY (SEQ ID NO: 204), and the VL domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASDLQS (SEQ ID NO: 206), and a CDR-L3 comprising the amino acid sequence of HQAYSFPFT (SEQ ID NO: 208);

(c) the VH domain comprises: a CDR-H1 comprising the amino acid sequence of DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence of WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence of NSGSASFGY (SEQ ID NO: 187), and the VL domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence of QQAYSFPFT (SEQ ID NO: 6);

(d) the VH domain comprises: a CDR-H1 comprising the amino acid sequence of DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence of WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence of NSGSYSAGY (SEQ ID NO: 190), and the VL domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence of QQAYSFPFT (SEQ ID NO: 6);

(e) the VH domain comprises: a CDR-H1 comprising the amino acid sequence of DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence of WINPNSGDTNYAQKFQG

(SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence of NSGSYSFGY (SEQ ID NO: 3), and the VL domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence of QAAYSFPFT (SEQ ID NO: 192); or

(f) the VH domain comprises: a CDR-H1 comprising the amino acid sequence of DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence of WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence of NSGSYSFGY (SEQ ID NO: 3), and the VL domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence of QQAYSAPFT (SEQ ID NO: 193).

28. The antibody of claim 26 or claim 27, wherein:

(a) the VH domain comprises the amino acid sequence of SEQ ID NO: 209, and the VL domain comprises the amino acid sequence of SEQ ID NO:210;

(b) the VH domain comprises the amino acid sequence of SEQ ID NO: 211, and the VL domain comprises the amino acid sequence of SEQ ID NO:212;

(c) the VH domain comprises the amino acid sequence of SEQ ID NO: 220, and the VL domain comprises the amino acid sequence of SEQ ID NO:221;

(d) the VH domain comprises the amino acid sequence of SEQ ID NO: 194, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(e) the VH domain comprises the amino acid sequence of SEQ ID NO: 196, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(f) the VH domain comprises the amino acid sequence of SEQ ID NO: 62, and the VL domain comprises the amino acid sequence of SEQ ID NO:197; or

(g) the VH domain comprises the amino acid sequence of SEQ ID NO: 62, and the VL domain comprises the amino acid sequence of SEQ ID NO:198.

29. The antibody of any one of claims 1-28, wherein the antibody or fragment binds to human Dectin-1 expressed on the surface of a macrophage, monocyte, dendritic cell, and/or granulocyte.

30. The antibody of any one of claims 1-29, wherein the antigen-binding antibody fragment is a Fab, Fab', F(ab')2, Fv, Fab'-SH, F(ab')2, single chain antibody, nanobody, or scFv fragment.

31. The antibody of any one of claims 1-29, wherein the antibody further comprises an Fc region.

32. The antibody of claim 31, wherein the Fc region is a human IgG Fc region.

33. The antibody of claim 32, wherein the Fc region is a human IgG1 or human IgG4 Fc region.

34. The antibody of claim 33, wherein the Fc region is:

(a) a human IgG1 Fc region comprising S239D and I332E substitutions, according to EU numbering;

(b) a human IgG1 Fc region comprising S239D, A330L, and I332E substitutions, according to EU numbering;

(c) a human IgG1 Fc region comprising G236A, S239D, A330L, and I332E substitutions, according to EU numbering; or

(d) a human IgG4 Fc region comprising an S228P substitution, according to EU numbering.

35. The antibody of claim 33, wherein the antibody comprises two antibody heavy chains, and wherein each of the antibody heavy chains comprises an amino acid substitution at one or more of positions 234, 235, and 237, according to EU numbering.

36. The antibody of claim 35, wherein each of the antibody heavy chains comprises L234A, L235E, and G237A substitutions, according to EU numbering.

37. The antibody of any one of claims 33-36, wherein the antibody comprises two antibody heavy chains, and wherein only one of the antibody heavy chains comprises H435R and Y436F substitutions, according to EU numbering.

38. The antibody of any one of claims 31-37, wherein the Fc region is non-fucosylated or comprises reduced fucosylation.

39. The antibody of any one of claims 1-38, wherein the antibody or fragment is a multispecific antibody or fragment.

40. The antibody of claim 39, wherein the antibody or fragment is a bispecific antibody, fragment, or diabody comprising a first antigen binding domain comprising the VH and VL domains that bind to human Dectin-1 and a second antigen binding domain comprising second VH and VL domains that bind to a target of interest.

41. The antibody of claim 40, wherein the bispecific antibody comprises a first IgG antibody comprising the first antigen binding domain covalently linked to a second IgG antibody comprising the second antigen binding domain.

42. The antibody of claim 40, wherein the bispecific antibody comprises a first antibody arm comprising a first antibody heavy chain that comprises the VH domain of the first antigen binding domain and a first Fc region, and a second antibody arm comprising a second antibody heavy chain that comprises the VH domain of the second antigen binding domain and a second Fc region, wherein the first Fc region comprises one or more knob-forming mutations, and the second Fc region comprises one or more cognate hole-forming mutations.

43. The antibody of claim 42, wherein the first Fc region comprises a T366W substitution, and wherein the second Fc region comprises T366S, L368A, and Y407V substitutions, according to EU numbering.

44. The antibody of claim 40, wherein the bispecific antibody comprises a first antibody arm comprising a first antibody heavy chain that comprises the VH domain of the first antigen binding domain and a first Fc region, and a second antibody arm comprising a second antibody heavy chain that comprises the VH domain of the second antigen binding domain and a second Fc region, wherein the first Fc region comprises one or more hole-forming mutations, and the second Fc region comprises one or more cognate knob-forming mutations.

45. The antibody of claim 44, wherein the first Fc region comprises T366S, L368A, and Y407V substitutions, and wherein the second Fc region comprises a T366W substitution, according to EU numbering.

46. The antibody of claim 40, wherein the bispecific antibody comprises a first antibody arm comprising a single chain variable fragment (scFv) comprising the VH and VL domains that bind to human Dectin-1 and a first Fc region, and a second antibody arm comprising an antibody heavy chain that comprises the VH domain of the second antigen binding domain in association with an antibody light chain that comprises the VL domain of the second antigen binding domain and a second Fc region connected to the VH domain of the second antigen binding domain.

47. The antibody of claim 46, wherein the first Fc region comprises one or more knob-forming mutations, and the second Fc region comprises one or more cognate hole-forming mutations, or wherein the second Fc region comprises one or more knob-forming mutations, and the first Fc region comprises one or more cognate hole-forming mutations.

48. The antibody of claim 46 or claim 47, wherein the first antibody arm comprises a first linker between the VH and VL domains, and a second linker between the VL domain and the first Fc region.

49. The antibody of claim 48, wherein the first linker comprises one or more repeats of the sequence GGGGS (SEQ ID NO:115).

50. The antibody of claim 49, wherein the first linker comprises the sequence GGGGSGGGGSGGGGS (SEQ ID NO:116) or GGGGSGGGGSGGGGSGGGGS (SEQ ID NO:117).

51. The antibody of any one of claims 48-50, wherein the second linker comprises the sequence EPKRSDKTHTCPPC (SEQ ID NO:118) or SATHTCPPC (SEQ ID NO:119).

52. The antibody of any one of claims 46-51, wherein the VH domain that binds to human Dectin-1 comprises the amino acid sequence of SEQ ID NO:220, and wherein the VL domain that binds to human Dectin-1 comprises the amino acid sequence of SEQ ID NO:221.

53. The antibody of claim 46, wherein the scFv comprises the amino acid sequence of SEQ ID NO:222.

54. The antibody of claim 46, wherein the first antibody arm comprises the amino acid sequence of SEQ ID NO:224 or 225.

55. The antibody of claim 40, wherein the bispecific antibody comprises a first IgG antibody comprising the first antigen binding domain coupled to biotin or an avidin-binding derivative

thereof, and a second IgG antibody comprising the second antigen binding domain coupled to avidin, streptavidin, neutravidin, or a biotin-binding derivative thereof, wherein the biotin or avidin-binding derivative thereof is bound to the avidin, streptavidin, neutravidin, or biotin-binding derivative thereof.

56. The antibody of claim 40, wherein the bispecific antibody comprises a first IgG antibody comprising the first antigen binding domain coupled to avidin, streptavidin, neutravidin, or a biotin-binding derivative thereof, and a second IgG antibody comprising the second antigen binding domain coupled to biotin or an avidin-binding derivative thereof, wherein the biotin or avidin-binding derivative thereof is bound to the avidin, streptavidin, neutravidin, or biotin-binding derivative thereof.

57. The antibody of claim 31, wherein the bispecific antibody comprises two antibody heavy chains and two antibody light chains, wherein the VH domain of the first antibody heavy chain forms an antigen binding domain with the VL domain of the first antibody light chain that binds human Dectin-1, wherein the VH domain of the second antibody heavy chain forms an antigen binding domain with the VL domain of the second antibody light chain that binds a target of interest; wherein the VH domain of the first antibody heavy chain comprises the amino acid sequence of SEQ ID NO:209, and wherein the VL domain of the first antibody light chain comprises the amino acid sequence of SEQ ID NO:210.

58. The antibody of claim 31, wherein the bispecific antibody comprises two antibody heavy chains and two antibody light chains, wherein the VH domain of the first antibody heavy chain forms an antigen binding domain with the VL domain of the first antibody light chain that binds human Dectin-1, wherein the VH domain of the second antibody heavy chain forms an antigen binding domain with the VL domain of the second antibody light chain that binds a target of interest; wherein the VH domain of the first antibody heavy chain comprises the amino acid sequence of SEQ ID NO:220, and wherein the VL domain of the first antibody light chain comprises the amino acid sequence of SEQ ID NO:221.

59. The antibody of claim 58, wherein the first antibody heavy chain comprises a C→S substitution at position 5, according to IMGT hinge numbering, and wherein the first antibody light chain comprises a C→S substitution at the terminal residue of the light chain constant domain.

60. The antibody of claim 58, wherein the first antibody heavy chain comprises the amino acid sequence of SEQ ID NO:219, and wherein the first antibody light chain comprises the amino acid sequence of SEQ ID NO:223.

61. The antibody of any one of claims 40-60, wherein the target of interest is a disease-causing agent.

62. The antibody of claim 61, wherein the disease-causing agent is a bacterial cell, fungal cell, virus, senescent cell, tumor cell, protein aggregate, LDL particle, mast cell, eosinophil, ILC2 cell, or inflammatory immune cell.

63. The antibody of claim 62, wherein the target of interest is an antigen expressed on the surface of the bacterial cell, fungal cell, senescent cell, tumor cell, mast cell, eosinophil, ILC2 cell, or inflammatory immune cell.

64. The antibody of claim 62, wherein the target of interest is a surface antigen of the virus.

65. The antibody of claim 61 or claim 62, wherein the target of interest is an antigen expressed on the surface of a cancer cell.

66. The antibody of claim 65, wherein the target of interest is CD70, HER2, DLL3, NECTIN-4, TROP-2, Mesothelin, LIV-1, C-MET, FOLR1, CD20, CCR8, CD33, or EGFR.

67. The antibody of claim 62, wherein the target of interest is amyloid beta, lambda light chain amyloid, or kappa light chain amyloid.

68. The antibody of any one of claims 31-67, wherein the antibody comprises two arms, wherein only one of the two antibody arms comprises a heavy chain comprising F126C and C220V substitutions and a light chain comprising S121C and C214V substitutions, according to EU numbering.

69. The antibody of claim 31, wherein the bispecific antibody comprises two antibody heavy chains and two antibody light chains, wherein the VH domain of the first antibody heavy chain forms an antigen binding domain with the VL domain of the first antibody light chain, wherein the VH domain of the second antibody heavy chain forms an antigen binding domain with the VL domain of the second antibody light chain, wherein the first antibody heavy chain comprises F126C, C220V, and T366W substitutions, wherein the first antibody light chain comprises

S121C and C214V substitutions, and wherein the second antibody heavy chain comprises T366S, L368A, Y407V, H435R, and Y436F substitutions, according to EU numbering.

70. The antibody of claim 69, wherein the first and second antibody heavy chains further comprise L234A, L235E, and G237A substitutions, according to EU numbering.

71. A multispecific binding molecule, comprising:

(a) a first antibody or antigen-binding fragment thereof comprising a first antigen binding domain, wherein the first antigen binding domain binds to human Dectin-1; and

(b) a second antibody or antigen-binding fragment thereof comprising a second antigen binding domain, wherein the second antigen binding domain binds to a target of interest;

wherein the first antigen binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain;

wherein the VH domain of the first antigen binding domain comprises the amino acid sequence QVQLVQSGAEVKKPGASVKVSCKSSGYTFTX$_1$YYIHWVRQAPGQGLEWMGWINPNSGX$_2$TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCAX$_3$X$_4$X$_5$X$_6$X$_7$X$_8$X$_9$X$_{10}$X$_{11}$X$_{12}$WGQGTLVTVSS, wherein X$_1$ is D, A, or G; wherein X$_2$ is D, A, or G; wherein X$_3$ is R, A, or G; wherein X$_4$ is N, A, or G; wherein X$_5$ is S, A, or G; wherein X$_6$ is A or G; wherein X$_7$ is S, A, or G; wherein X$_8$ is Y, A, or G; wherein X$_9$ is S, A, or G; wherein X$_{10}$ is F, A, or G; wherein X$_{11}$ is A or G; and wherein X$_{12}$ is Y, A, or G (SEQ ID NO:63); and

wherein the VL domain of the first antigen binding domain comprises the amino acid sequence DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPSRFSGSGSGTDFTLTVSSLQPEDFATYYCX$_1$X$_2$AX$_3$X$_4$X$_5$X$_6$X$_7$X$_8$FGPGTKVDIE, wherein X$_1$ is Q, A, or G; X$_2$ is Q, A, or G; X$_3$ is F, Y, A, or G; wherein X$_4$ is S, A, or G; wherein X$_5$ is F, A, or G; wherein X$_6$ is P, A, or G; wherein X$_7$ is F, A, or G; and wherein X$_8$ is T, A, or G (SEQ ID NO:65).

72. The multispecific binding molecule of claim 71, wherein the antibody does not comprise a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), a CDR-H3 comprising

the amino acid sequence NSGSYSFGY (SEQ ID NO: 3), a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6).

73. The multispecific binding molecule of claim 71 or claim 72, wherein the VH domain of the first antigen binding domain comprises 1, 2 or fewer, 3 or fewer, 4 or fewer, or 5 or fewer substitutions as compared to the amino acid sequence of SEQ ID NO:62; and/or wherein the VL domain of the first antigen binding domain comprises 1, 2 or fewer, 3 or fewer, 4 or fewer, or 5 or fewer substitutions as compared to the amino acid sequence of SEQ ID NO:64.

74. The multispecific binding molecule of any one of claims 71-73, wherein the first antigen binding domain:

(a) binds to human Dectin-1 expressed on the surface of a cell with an EC50 of less than 2nM;

(b) is capable of binding human or cynomolgus Dectin-1; and/or

(c) does not compete with a native ligand of human Dectin-1.

75. A multispecific binding molecule, comprising:

(a) a first antibody or antigen-binding fragment thereof comprising a first antigen binding domain, wherein the first antigen binding domain binds to human Dectin-1; and

(b) a second antibody or antigen-binding fragment thereof comprising a second antigen binding domain, wherein the second antigen binding domain binds to a target of interest;

wherein the first antigen binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain;

wherein the VH domain of the first antigen binding domain comprises: a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1) or AYYI (SEQ ID NO: 16); a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2) or WINPNSGATNYAQKFQG (SEQ ID NO: 19); and a CDR-H3 comprising an amino acid sequence selected from the group consisting of NSGSYSFGY (SEQ ID NO: 3), ASGSYSFGY (SEQ ID NO: 22), NSGSASFGY (SEQ ID NO: 24), NAGSYSFGY (SEQ ID NO: 27),

NSASYSFGY (SEQ ID NO: 29), NSGAYSFGY (SEQ ID NO: 31), NSGSYAFGY (SEQ ID NO: 33), NSGSYSAGY (SEQ ID NO: 35), NSGSYSFAY (SEQ ID NO: 37), and NSGSYSFGA (SEQ ID NO: 39); and

wherein the VL domain of the first antigen binding domain comprises: a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4); a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising an amino acid sequence selected from the group consisting of QQAYSFPFT (SEQ ID NO: 6), QQAASFPFT (SEQ ID NO: 41), QQAFSFPFT (SEQ ID NO: 42), AQAYSFPFT (SEQ ID NO: 43), QAAYSFPFT (SEQ ID NO: 44), QQAYAFPFT (SEQ ID NO: 45), QQAYSAPFT (SEQ ID NO: 46), QQAYSFAFT (SEQ ID NO: 47), QQAYSFPAT (SEQ ID NO: 48), and QQAYSFPFA (SEQ ID NO: 49).

76. The multispecific binding molecule of claim 75, wherein the antibody does not comprise a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3), a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6).

77. The multispecific binding molecule of any one of claims 71-76, wherein the VH domain of the first antigen binding domain comprises:

(a) a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3);

(b) a CDR-H1 comprising the amino acid sequence AYYI (SEQ ID NO: 16), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3);

(c) a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGATNYAQKFQG (SEQ ID NO: 19), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3);

(d) a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence ASGSYSFGY (SEQ ID NO: 22);

(e) a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSASFGY (SEQ ID NO: 24);

(f) a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NAGSYSFGY (SEQ ID NO: 27);

(g) a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSASYSFGY (SEQ ID NO: 29);

(h) a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGAYSFGY (SEQ ID NO: 31);

(i) a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYAFGY (SEQ ID NO: 33);

(j) a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSAGY (SEQ ID NO: 35);

(k) a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSFAY (SEQ ID NO: 37); or

(l) a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSFGA (SEQ ID NO: 39).

78. The multispecific binding molecule of any one of claims 71-77, wherein the VH domain of the first antigen binding domain further comprises:

(a) a FR1 comprising an amino acid sequence selected from the group consisting of QVQLVQSGAEVKKPGASVKVSCKSSGYTFT (SEQ ID NO:50) and QVQLVQSGAEVKKPGASVKVSCKASGYTFT (SEQ ID NO:51);

(b) a FR2 comprising the amino acid sequence HWVRQAPGQGLEWMG (SEQ ID NO:52);

(c) a FR3 comprising an amino acid sequence selected from the group consisting of RITMTRDTSISTAYLELSRLRSDDTAVFYCAR (SEQ ID NO:53) and RVTMTRDTSISTAYMELSRLRSDDTAVYYCAR (SEQ ID NO:54); and

(d) a FR4 comprising the amino acid sequence WGQGTLVTVSS (SEQ ID NO:55)

79. The multispecific binding molecule of any one of claims 71-78, wherein the VH domain of the first antigen binding domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos:62 and 82-93.

80. The multispecific binding molecule of any one of claims 71-79, wherein the VL domain of the first antigen binding domain comprises:

(a) a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6);

(b) a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAASFPFT (SEQ ID NO: 41);

(c) a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAFSFPFT (SEQ ID NO: 42);

(d) a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence AQAYSFPFT (SEQ ID NO: 43);

(e) a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QAAYSFPFT (SEQ ID NO: 44);

(f) a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYAFPFT (SEQ ID NO: 45);

(g) a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSAPFT (SEQ ID NO: 46);

(h) a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFAFT (SEQ ID NO: 47);

(i) a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPAT (SEQ ID NO: 48); or

(j) a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFA (SEQ ID NO: 49).

81. The multispecific binding molecule of any one of claims 71-80, wherein the VL domain of the first antigen binding domain further comprises:

(a) a FR1 comprising the amino acid sequence DIQMTQSPSSVSASVGDRVTITC (SEQ ID NO:56);

(b) a FR2 comprising an amino acid sequence selected from the group consisting of WYQQKPGKAPKLLIF (SEQ ID NO:57) and WYQQKPGKAPKLLIY (SEQ ID NO:58);

(c) a FR3 comprising an amino acid sequence selected from the group consisting of GVPSRFSGSGSGTDFTLTVSSLQPEDFATYYC (SEQ ID NO:59) and GVPSRFSGSGSGTDFTLTISSLQPEDFATYYC (SEQ ID NO:60); and

(d) a FR4 comprising the amino acid sequence FGPGTKVDIE (SEQ ID NO:61).

82. The multispecific binding molecule of any one of claims 71-81, wherein the VL domain of the first antigen binding domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos: 64 and 94-102.

83. The multispecific binding molecule of any one of claims 71-76, wherein, in the first antigen binding domain:

(1) the VH domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain comprises the amino acid sequence of SEQ ID NO:94;

(2) the VH domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain comprises the amino acid sequence of SEQ ID NO:95;

(3) the VH domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain comprises the amino acid sequence of SEQ ID NO:96;

(4) the VH domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain comprises the amino acid sequence of SEQ ID NO:97;

(5) the VH domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain comprises the amino acid sequence of SEQ ID NO:98;

(6) the VH domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain comprises the amino acid sequence of SEQ ID NO:99;

(7) the VH domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain comprises the amino acid sequence of SEQ ID NO:100;

(8) the VH domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain comprises the amino acid sequence of SEQ ID NO:101;

(9) the VH domain comprises the amino acid sequence of SEQ ID NO:62, and the VL domain comprises the amino acid sequence of SEQ ID NO:102;

(10) the VH domain comprises the amino acid sequence of SEQ ID NO:82, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(11) the VH domain comprises the amino acid sequence of SEQ ID NO:82, and the VL domain comprises the amino acid sequence of SEQ ID NO:94;

(12) the VH domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain comprises the amino acid sequence of SEQ ID NO:95;

(13) the VH domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain comprises the amino acid sequence of SEQ ID NO:96;

(14) the VH domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain comprises the amino acid sequence of SEQ ID NO:97;

(15) the VH domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain comprises the amino acid sequence of SEQ ID NO:98;

(16) the VH domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain comprises the amino acid sequence of SEQ ID NO:99;

(17) the VH domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain comprises the amino acid sequence of SEQ ID NO:100;

(18) the VH domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain comprises the amino acid sequence of SEQ ID NO:101;

(19) the VH domain comprises the amino acid sequence of SEQ ID NO: 82, and the VL domain comprises the amino acid sequence of SEQ ID NO:102;

(20) the VH domain comprises the amino acid sequence of SEQ ID NO:83, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(21) the VH domain comprises the amino acid sequence of SEQ ID NO:83, and the VL domain comprises the amino acid sequence of SEQ ID NO:94;

(22) the VH domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain comprises the amino acid sequence of SEQ ID NO:95;

(23) the VH domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain comprises the amino acid sequence of SEQ ID NO:96;

(24) the VH domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain comprises the amino acid sequence of SEQ ID NO:97;

(25) the VH domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain comprises the amino acid sequence of SEQ ID NO:98;

(26) the VH domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain comprises the amino acid sequence of SEQ ID NO:99;

(27) the VH domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain comprises the amino acid sequence of SEQ ID NO:100;

(28) the VH domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain comprises the amino acid sequence of SEQ ID NO:101;

(29) the VH domain comprises the amino acid sequence of SEQ ID NO: 83, and the VL domain comprises the amino acid sequence of SEQ ID NO:102;

(30) the VH domain comprises the amino acid sequence of SEQ ID NO:84, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(31) the VH domain comprises the amino acid sequence of SEQ ID NO:84, and the VL domain comprises the amino acid sequence of SEQ ID NO:94;

(32) the VH domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain comprises the amino acid sequence of SEQ ID NO:95;

(33) the VH domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain comprises the amino acid sequence of SEQ ID NO:96;

(34) the VH domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain comprises the amino acid sequence of SEQ ID NO:97;

(35) the VH domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain comprises the amino acid sequence of SEQ ID NO:98;

(36) the VH domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain comprises the amino acid sequence of SEQ ID NO:99;

(37) the VH domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain comprises the amino acid sequence of SEQ ID NO:100;

(38) the VH domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain comprises the amino acid sequence of SEQ ID NO:101;

(39) the VH domain comprises the amino acid sequence of SEQ ID NO: 84, and the VL domain comprises the amino acid sequence of SEQ ID NO:102;

(40) the VH domain comprises the amino acid sequence of SEQ ID NO:85, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(41) the VH domain comprises the amino acid sequence of SEQ ID NO:85, and the VL domain comprises the amino acid sequence of SEQ ID NO:94;

(42) the VH domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain comprises the amino acid sequence of SEQ ID NO:95;

(43) the VH domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain comprises the amino acid sequence of SEQ ID NO:96;

(44) the VH domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain comprises the amino acid sequence of SEQ ID NO:97;

(45) the VH domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain comprises the amino acid sequence of SEQ ID NO:98;

(46) the VH domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain comprises the amino acid sequence of SEQ ID NO:99;

(47) the VH domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain comprises the amino acid sequence of SEQ ID NO:100;

(48) the VH domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain comprises the amino acid sequence of SEQ ID NO:101;

(49) the VH domain comprises the amino acid sequence of SEQ ID NO: 85, and the VL domain comprises the amino acid sequence of SEQ ID NO:102;

(50) the VH domain comprises the amino acid sequence of SEQ ID NO:86, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(51) the VH domain comprises the amino acid sequence of SEQ ID NO:86, and the VL domain comprises the amino acid sequence of SEQ ID NO:94;

(52) the VH domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain comprises the amino acid sequence of SEQ ID NO:95;

(53) the VH domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain comprises the amino acid sequence of SEQ ID NO:96;

(54) the VH domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain comprises the amino acid sequence of SEQ ID NO:97;

(55) the VH domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain comprises the amino acid sequence of SEQ ID NO:98;

(56) the VH domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain comprises the amino acid sequence of SEQ ID NO:99;

(57) the VH domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain comprises the amino acid sequence of SEQ ID NO:100;

(58) the VH domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain comprises the amino acid sequence of SEQ ID NO:101;

(59) the VH domain comprises the amino acid sequence of SEQ ID NO: 86, and the VL domain comprises the amino acid sequence of SEQ ID NO:102;

(60) the VH domain comprises the amino acid sequence of SEQ ID NO:87, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(61) the VH domain comprises the amino acid sequence of SEQ ID NO:87, and the VL domain comprises the amino acid sequence of SEQ ID NO:94;

(62) the VH domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain comprises the amino acid sequence of SEQ ID NO:95;

(63) the VH domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain comprises the amino acid sequence of SEQ ID NO:96;

(64) the VH domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain comprises the amino acid sequence of SEQ ID NO:97;

(65) the VH domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain comprises the amino acid sequence of SEQ ID NO:98;

(66) the VH domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain comprises the amino acid sequence of SEQ ID NO:99;

(67) the VH domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain comprises the amino acid sequence of SEQ ID NO:100;

(68) the VH domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain comprises the amino acid sequence of SEQ ID NO:101;

(69) the VH domain comprises the amino acid sequence of SEQ ID NO: 87, and the VL domain comprises the amino acid sequence of SEQ ID NO:102;

(70) the VH domain comprises the amino acid sequence of SEQ ID NO:88, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(71) the VH domain comprises the amino acid sequence of SEQ ID NO:88, and the VL domain comprises the amino acid sequence of SEQ ID NO:94;

(72) the VH domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain comprises the amino acid sequence of SEQ ID NO:95;

(73) the VH domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain comprises the amino acid sequence of SEQ ID NO:96;

(74) the VH domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain comprises the amino acid sequence of SEQ ID NO:97;

(75) the VH domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain comprises the amino acid sequence of SEQ ID NO:98;

(76) the VH domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain comprises the amino acid sequence of SEQ ID NO:99;

(77) the VH domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain comprises the amino acid sequence of SEQ ID NO:100;

(78) the VH domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain comprises the amino acid sequence of SEQ ID NO:101;

(79) the VH domain comprises the amino acid sequence of SEQ ID NO: 88, and the VL domain comprises the amino acid sequence of SEQ ID NO:102;

(80) the VH domain comprises the amino acid sequence of SEQ ID NO:89, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(81) the VH domain comprises the amino acid sequence of SEQ ID NO:89, and the VL domain comprises the amino acid sequence of SEQ ID NO:94;

(82) the VH domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain comprises the amino acid sequence of SEQ ID NO:95;

(83) the VH domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain comprises the amino acid sequence of SEQ ID NO:96;

(84) the VH domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain comprises the amino acid sequence of SEQ ID NO:97;

(85) the VH domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain comprises the amino acid sequence of SEQ ID NO:98;

(86) the VH domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain comprises the amino acid sequence of SEQ ID NO:99;

(87) the VH domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain comprises the amino acid sequence of SEQ ID NO:100;

(88) the VH domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain comprises the amino acid sequence of SEQ ID NO:101;

(89) the VH domain comprises the amino acid sequence of SEQ ID NO: 89, and the VL domain comprises the amino acid sequence of SEQ ID NO:102;

(90) the VH domain comprises the amino acid sequence of SEQ ID NO:90, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(91) the VH domain comprises the amino acid sequence of SEQ ID NO:90, and the VL domain comprises the amino acid sequence of SEQ ID NO:94;

(92) the VH domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain comprises the amino acid sequence of SEQ ID NO:95;

(93) the VH domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain comprises the amino acid sequence of SEQ ID NO:96;

(94) the VH domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain comprises the amino acid sequence of SEQ ID NO:97;

(95) the VH domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain comprises the amino acid sequence of SEQ ID NO:98;

(96) the VH domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain comprises the amino acid sequence of SEQ ID NO:99;

(97) the VH domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain comprises the amino acid sequence of SEQ ID NO:100;

(98) the VH domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain comprises the amino acid sequence of SEQ ID NO:101;

(99) the VH domain comprises the amino acid sequence of SEQ ID NO: 90, and the VL domain comprises the amino acid sequence of SEQ ID NO:102;

(100) the VH domain comprises the amino acid sequence of SEQ ID NO:91, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(101) the VH domain comprises the amino acid sequence of SEQ ID NO:91, and the VL domain comprises the amino acid sequence of SEQ ID NO:94;

(102) the VH domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain comprises the amino acid sequence of SEQ ID NO:95;

(103) the VH domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain comprises the amino acid sequence of SEQ ID NO:96;

(104) the VH domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain comprises the amino acid sequence of SEQ ID NO:97;

(105) the VH domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain comprises the amino acid sequence of SEQ ID NO:98;

(106) the VH domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain comprises the amino acid sequence of SEQ ID NO:99;

(107) the VH domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain comprises the amino acid sequence of SEQ ID NO:100;

(108) the VH domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain comprises the amino acid sequence of SEQ ID NO:101;

(109) the VH domain comprises the amino acid sequence of SEQ ID NO: 91, and the VL domain comprises the amino acid sequence of SEQ ID NO:102;

(110) the VH domain comprises the amino acid sequence of SEQ ID NO:92, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(111) the VH domain comprises the amino acid sequence of SEQ ID NO:92, and the VL domain comprises the amino acid sequence of SEQ ID NO:94;

(112) the VH domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain comprises the amino acid sequence of SEQ ID NO:95;

(113) the VH domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain comprises the amino acid sequence of SEQ ID NO:96;

(114) the VH domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain comprises the amino acid sequence of SEQ ID NO:97;

(115) the VH domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain comprises the amino acid sequence of SEQ ID NO:98;

(116) the VH domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain comprises the amino acid sequence of SEQ ID NO:99;

(117) the VH domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain comprises the amino acid sequence of SEQ ID NO:100;

(118) the VH domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain comprises the amino acid sequence of SEQ ID NO:101;

(119) the VH domain comprises the amino acid sequence of SEQ ID NO: 92, and the VL domain comprises the amino acid sequence of SEQ ID NO:102;

(120) the VH domain comprises the amino acid sequence of SEQ ID NO:93, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(121) the VH domain comprises the amino acid sequence of SEQ ID NO:93, and the VL domain comprises the amino acid sequence of SEQ ID NO:94;

(122) the VH domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain comprises the amino acid sequence of SEQ ID NO:95;

(123) the VH domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain comprises the amino acid sequence of SEQ ID NO:96;

(124) the VH domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain comprises the amino acid sequence of SEQ ID NO:97;

(125) the VH domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain comprises the amino acid sequence of SEQ ID NO:98;

(126) the VH domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain comprises the amino acid sequence of SEQ ID NO:99;

(127) the VH domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain comprises the amino acid sequence of SEQ ID NO:100;

(128) the VH domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain comprises the amino acid sequence of SEQ ID NO:101; or

(129) the VH domain comprises the amino acid sequence of SEQ ID NO: 93, and the VL domain comprises the amino acid sequence of SEQ ID NO:102

84. A multispecific binding molecule, comprising:

(a) a first antibody or antigen-binding fragment thereof comprising a first antigen binding domain, wherein the first antigen binding domain binds to human Dectin-1; and

(b) a second antibody or antigen-binding fragment thereof comprising a second antigen binding domain, wherein the second antigen binding domain binds to a target of interest;

wherein the first antigen binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain;

wherein the VH domain of the first antigen binding domain comprises the amino acid sequence QVQLVQSGAEVKKPGASVKVSCKX$_1$SGYTFTX$_2$YYX$_3$HWVRQAPGQGLEWMGWINPNSGX$_4$TNYAQKFQGRX$_5$TMTRDTSISTAYX$_6$ELSRLRSDDTAVX$_7$YCARNSGSYSFGYWGQGTLVTVSS; wherein X$_1$ is S or A; wherein X$_2$ is D or G; wherein X$_3$ is I or M; wherein X$_4$ is D or G; wherein X$_5$ is I or V; wherein X$_6$ is L or M; and wherein X$_7$ is F or Y (SEQ ID NO:80); and

wherein the VL domain of the first antigen binding domain comprises the amino acid sequence DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIX$_1$X$_2$ASSLQSGVPSRFSGSGSGTDFTLTX$_3$SSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE; wherein X$_1$ is F or Y; wherein X$_2$ is G or A; and wherein X$_3$ is V or I (SEQ ID NO:81).

85. A multispecific binding molecule, comprising:

(a) a first antibody or antigen-binding fragment thereof comprising a first antigen binding domain, wherein the first antigen binding domain binds to human Dectin-1; and

(b) a second antibody or antigen-binding fragment thereof comprising a second antigen binding domain, wherein the second antigen binding domain binds to a target of interest;

wherein the first antigen binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain;

wherein the VH domain of the first antigen binding domain comprises: a CDR-H1 comprising an amino acid sequence selected from the group consisting of DYYI (SEQ ID NO: 1), DYYM (SEQ ID NO: 66), and GYYM (SEQ ID NO: 67); a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2) or WINPNSGGTNYAQKFQG (SEQ ID NO: 70); and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3); and

wherein the VL domain of the first antigen binding domain comprises: a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4); a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5) or AASSLQS (SEQ ID NO: 73), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6).

86. The multispecific binding molecule of claim 84 or claim 85, wherein the antibody does not comprise a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3), a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6).

87. The multispecific binding molecule of any one of claims 84-86, wherein the VH domain of the first antigen binding domain comprises:

(a) a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3);

(b) a CDR-H1 comprising the amino acid sequence DYYM (SEQ ID NO: 66), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3);

(c) a CDR-H1 comprising the amino acid sequence GYYM (SEQ ID NO: 67), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3);

(d) a CDR-H1 comprising the amino acid sequence DYYM (SEQ ID NO: 66), a CDR-H2 comprising the amino acid sequence WINPNSGGTNYAQKFQG (SEQ ID NO: 70), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3); or

(e) a CDR-H1 comprising the amino acid sequence GYYM (SEQ ID NO: 67), a CDR-H2 comprising the amino acid sequence WINPNSGGTNYAQKFQG (SEQ ID NO: 70), and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3).

88. The multispecific binding molecule of any one of claims 84-87, wherein the VH domain of the first antigen binding domain further comprises:

(a) a FR1 comprising an amino acid sequence selected from the group consisting of QVQLVQSGAEVKKPGASVKVSCKSSGYTFT (SEQ ID NO:50) and QVQLVQSGAEVKKPGASVKVSCKASGYTFT (SEQ ID NO:76);

(b) a FR2 comprising the amino acid sequence HWVRQAPGQGLEWMG (SEQ ID NO:52);

(c) a FR3 comprising an amino acid sequence selected from the group consisting of RITMTRDTSISTAYLELSRLRSDDTAVFYCAR (SEQ ID NO:53) and RVTMTRDTSISTAYMELSRLRSDDTAVYYCAR (SEQ ID NO:77); and

(d) a FR4 comprising the amino acid sequence WGQGTLVTVSS (SEQ ID NO:55).

89. The multispecific binding molecule of any one of claims 84-88, wherein the VH domain of the first antigen binding domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos: 62 and 103-109.

90. The multispecific binding molecule of any one of claims 84-89, wherein the VL domain of the first antigen binding domain comprises:

(a) a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6); or

(b) a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence AASSLQS (SEQ ID NO: 73), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6).

91. The multispecific binding molecule of any one of claims 84-90, wherein the VL domain of the first antigen binding domain further comprises:

(a) a FR1 comprising the amino acid sequence DIQMTQSPSSVSASVGDRVTITC (SEQ ID NO:56);

(b) a FR2 comprising an amino acid sequence selected from the group consisting of WYQQKPGKAPKLLIF (SEQ ID NO:57) and WYQQKPGKAPKLLIY (SEQ ID NO:78);

(c) a FR3 comprising an amino acid sequence selected from the group consisting of GVPSRFSGSGSGTDFTLTVSSLQPEDFATYYC (SEQ ID NO:59) and GVPSRFSGSGSGTDFTLTISSLQPEDFATYYC (SEQ ID NO:79); and

(d) a FR4 comprising the amino acid sequence FGPGTKVDIE (SEQ ID NO:61).

92. The multispecific binding molecule of any one of claims 84-91, wherein the VL domain of the first antigen binding domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos:64 and 110-113.

93. The multispecific binding molecule of any one of claims 84-86, wherein, in the first antigen binding domain:

(1) the VH domain comprises the amino acid sequence of SEQ ID NO: 62, and the VL domain comprises the amino acid sequence of SEQ ID NO:110;

(2) the VH domain comprises the amino acid sequence of SEQ ID NO: 62, and the VL domain comprises the amino acid sequence of SEQ ID NO:111;

(3) the VH domain comprises the amino acid sequence of SEQ ID NO: 62, and the VL domain comprises the amino acid sequence of SEQ ID NO:112;

(4) the VH domain comprises the amino acid sequence of SEQ ID NO: 62, and the VL domain comprises the amino acid sequence of SEQ ID NO:113;

(5) the VH domain comprises the amino acid sequence of SEQ ID NO: 103, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(6) the VH domain comprises the amino acid sequence of SEQ ID NO: 103, and the VL domain comprises the amino acid sequence of SEQ ID NO:110;

(7) the VH domain comprises the amino acid sequence of SEQ ID NO: 103, and the VL domain comprises the amino acid sequence of SEQ ID NO:111;

(8) the VH domain comprises the amino acid sequence of SEQ ID NO: 103, and the VL domain comprises the amino acid sequence of SEQ ID NO:112;

(9) the VH domain comprises the amino acid sequence of SEQ ID NO: 103, and the VL domain comprises the amino acid sequence of SEQ ID NO:113;

(10) the VH domain comprises the amino acid sequence of SEQ ID NO: 104, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(11) the VH domain comprises the amino acid sequence of SEQ ID NO: 104, and the VL domain comprises the amino acid sequence of SEQ ID NO:110;

(12) the VH domain comprises the amino acid sequence of SEQ ID NO: 104, and the VL domain comprises the amino acid sequence of SEQ ID NO:111;

(13) the VH domain comprises the amino acid sequence of SEQ ID NO: 104, and the VL domain comprises the amino acid sequence of SEQ ID NO:112;

(14) the VH domain comprises the amino acid sequence of SEQ ID NO: 104, and the VL domain comprises the amino acid sequence of SEQ ID NO:113;

(15) the VH domain comprises the amino acid sequence of SEQ ID NO: 105, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(16) the VH domain comprises the amino acid sequence of SEQ ID NO: 105, and the VL domain comprises the amino acid sequence of SEQ ID NO:110;

(17) the VH domain comprises the amino acid sequence of SEQ ID NO: 105, and the VL domain comprises the amino acid sequence of SEQ ID NO:111;

(18) the VH domain comprises the amino acid sequence of SEQ ID NO: 105, and the VL domain comprises the amino acid sequence of SEQ ID NO:112;

(19) the VH domain comprises the amino acid sequence of SEQ ID NO: 105, and the VL domain comprises the amino acid sequence of SEQ ID NO:113;

(20) the VH domain comprises the amino acid sequence of SEQ ID NO: 106, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(21) the VH domain comprises the amino acid sequence of SEQ ID NO: 106, and the VL domain comprises the amino acid sequence of SEQ ID NO:110;

(22) the VH domain comprises the amino acid sequence of SEQ ID NO: 106, and the VL domain comprises the amino acid sequence of SEQ ID NO:111;

(23) the VH domain comprises the amino acid sequence of SEQ ID NO: 106, and the VL domain comprises the amino acid sequence of SEQ ID NO:112;

(24) the VH domain comprises the amino acid sequence of SEQ ID NO: 106, and the VL domain comprises the amino acid sequence of SEQ ID NO:113;

(25) the VH domain comprises the amino acid sequence of SEQ ID NO: 107, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(26) the VH domain comprises the amino acid sequence of SEQ ID NO: 107, and the VL domain comprises the amino acid sequence of SEQ ID NO:110;

(27) the VH domain comprises the amino acid sequence of SEQ ID NO: 107, and the VL domain comprises the amino acid sequence of SEQ ID NO:111;

(28) the VH domain comprises the amino acid sequence of SEQ ID NO: 107, and the VL domain comprises the amino acid sequence of SEQ ID NO:112;

(29) the VH domain comprises the amino acid sequence of SEQ ID NO: 107, and the VL domain comprises the amino acid sequence of SEQ ID NO:113;

(30) the VH domain comprises the amino acid sequence of SEQ ID NO: 108, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(31) the VH domain comprises the amino acid sequence of SEQ ID NO: 108, and the VL domain comprises the amino acid sequence of SEQ ID NO:110;

(32) the VH domain comprises the amino acid sequence of SEQ ID NO: 108, and the VL domain comprises the amino acid sequence of SEQ ID NO:111;

(33) the VH domain comprises the amino acid sequence of SEQ ID NO: 108, and the VL domain comprises the amino acid sequence of SEQ ID NO:112;

(34) the VH domain comprises the amino acid sequence of SEQ ID NO: 108, and the VL domain comprises the amino acid sequence of SEQ ID NO:113;

(35) the VH domain comprises the amino acid sequence of SEQ ID NO: 109, and the VL domain comprises the amino acid sequence of SEQ ID NO:64;

(36) the VH domain comprises the amino acid sequence of SEQ ID NO: 109, and the VL domain comprises the amino acid sequence of SEQ ID NO:110;

(37) the VH domain comprises the amino acid sequence of SEQ ID NO: 109, and the VL domain comprises the amino acid sequence of SEQ ID NO:111;

(38) the VH domain comprises the amino acid sequence of SEQ ID NO: 109, and the VL domain comprises the amino acid sequence of SEQ ID NO:112; or

(39) the VH domain comprises the amino acid sequence of SEQ ID NO: 109, and the VL domain comprises the amino acid sequence of SEQ ID NO:113.

94. The multispecific binding molecule of claim 85, wherein the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 213, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:214.

95. The multispecific binding molecule of claim 85, wherein the VH domain comprises the amino acid sequence of SEQ ID NO: 195, and the VL domain comprises the amino acid sequence of SEQ ID NO:64.

96. A multispecific binding molecule, comprising:

(a) a first antibody or antigen-binding fragment thereof comprising a first antigen binding domain, wherein the first antigen binding domain binds to human Dectin-1; and

(b) a second antibody or antigen-binding fragment thereof comprising a second antigen binding domain, wherein the second antigen binding domain binds to a target of interest;

wherein the first antigen binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain;

wherein the VH domain of the first antigen binding domain comprises: a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1) or DYYM (SEQ ID NO: 199); a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), WINPNEGDTNYAQKFEG (SEQ ID NO: 200), or WINPNEGDTNYAQKFQE (SEQ ID NO: 201); and a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3), NSGSASFGY (SEQ ID NO: 187), NSGSYSAGY (SEQ ID NO: 190), or NTGAYSFGY (SEQ ID NO: 204); and

wherein the VL domain of the first antigen binding domain comprises: a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4); a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5) or GASDLQS (SEQ ID NO: 206), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6), QAAYSFPFT (SEQ ID NO: 192), QQAYSAPFT (SEQ ID NO: 193), QQAYGFPFT (SEQ ID NO: 207), or HQAYSFPFT (SEQ ID NO: 208);

wherein the multispecific binding molecule does not comprise a CDR-H1 comprising the amino acid sequence DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence WINPNSGDTNYAQKFQG (SEQ ID NO: 2), a CDR-H3 comprising the amino acid sequence NSGSYSFGY (SEQ ID NO: 3), a CDR-L1 comprising the amino acid sequence RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQAYSFPFT (SEQ ID NO: 6).

97. The multispecific binding molecule of claim 96, wherein:

(a) the VH domain of the first antigen binding domain comprises: a CDR-H1 comprising the amino acid sequence of DYYM (SEQ ID NO: 199), a CDR-H2 comprising the amino acid sequence of WINPNEGDTNYAQKFEG (SEQ ID NO: 200), and a CDR-H3 comprising the amino acid sequence of NTGAYSFGY (SEQ ID NO: 204), and the VL domain of the first antigen binding domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASDLQS (SEQ ID NO: 206), and a CDR-L3 comprising the amino acid sequence of QQAYGFPFT (SEQ ID NO: 207);

(b) the VH domain of the first antigen binding domain comprises: a CDR-H1 comprising the amino acid sequence of DYYM (SEQ ID NO: 199), a CDR-H2 comprising the amino acid sequence of WINPNEGDTNYAQKFQE (SEQ ID NO: 201), and a CDR-H3 comprising the amino acid sequence of NTGAYSFGY (SEQ ID NO: 204), and the VL domain of the first antigen binding domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASDLQS (SEQ ID NO: 206), and a CDR-L3 comprising the amino acid sequence of HQAYSFPFT (SEQ ID NO: 208);

(c) the VH domain of the first antigen binding domain comprises: a CDR-H1 comprising the amino acid sequence of DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence of WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence of NSGSASFGY (SEQ ID NO: 187), and the VL domain of the first antigen binding domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence of QQAYSFPFT (SEQ ID NO: 6);

(d) the VH domain of the first antigen binding domain comprises: a CDR-H1 comprising the amino acid sequence of DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence of WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence of NSGSYSAGY (SEQ ID NO: 190), and the VL domain of the first antigen binding domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence of QQAYSFPFT (SEQ ID NO: 6);

(e) the VH domain of the first antigen binding domain comprises: a CDR-H1 comprising the amino acid sequence of DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence of WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence of NSGSYSFGY (SEQ ID NO: 3), and the VL domain of the first antigen binding domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence of QAAYSFPFT (SEQ ID NO: 192); or

(f) the VH domain of the first antigen binding domain comprises: a CDR-H1 comprising the amino acid sequence of DYYI (SEQ ID NO: 1), a CDR-H2 comprising the amino acid

sequence of WINPNSGDTNYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence of NSGSYSFGY (SEQ ID NO: 3), and the VL domain of the first antigen binding domain comprises: a CDR-L1 comprising the amino acid sequence of RASQGISSWLA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence of GASSLQS (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence of QQAYSAPFT (SEQ ID NO: 193).

98. The multispecific binding molecule of claim 96 or claim 97, wherein:

(a) the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 209, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:210;

(b) the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 211, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:212;

(c) the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 220, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:221;

(d) the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 194, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:64;

(e) the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 196, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:64;

(f) the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 62, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:197; or

(g) the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 62, and the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:198.

99. The multispecific binding molecule of any one of claims 71-98, wherein the target of interest is a disease-causing agent.

100. The multispecific binding molecule of claim 99, wherein the disease-causing agent is a bacterial cell, fungal cell, virus, senescent cell, tumor cell, protein aggregate, LDL particle, mast cell, eosinophil, ILC2 cell, or inflammatory immune cell.

101. The multispecific binding molecule of claim 100, wherein the target of interest is an antigen expressed on the surface of the bacterial cell, fungal cell, senescent cell, tumor cell, mast cell, eosinophil, ILC2 cell, or inflammatory immune cell.

102. The multispecific binding molecule of claim 100, wherein the target of interest is a surface antigen of the virus.

103. The multispecific binding molecule of claim 99 or claim 100, wherein the target of interest is an antigen expressed on the surface of a cancer cell.

104. The multispecific binding molecule of claim 103, wherein the target of interest is CD70, HER2, DLL3, NECTIN-4, TROP-2, Mesothelin, LIV-1, C-MET, FOLR1, CD20, CCR8, CD33, or EGFR.

105. The multispecific binding molecule of claim 100, wherein the target of interest is amyloid beta, lambda light chain amyloid, or kappa light chain amyloid.

106. The multispecific binding molecule of any one of claims 71-98, wherein the second antigen-binding domain binds to CD20 and comprises a VH domain comprising the sequence of SEQ ID NO:129 and a VL domain comprising the sequence of SEQ ID NO:130.

107. The multispecific binding molecule of any one of claims 71-98, wherein the second antigen-binding domain binds to Trop-2 and comprises a VH domain comprising the sequence of SEQ ID NO:139 and a VL domain comprising the sequence of SEQ ID NO:140.

108. The multispecific binding molecule of any one of claims 71-98, wherein the second antigen-binding domain binds to light chain amyloid and comprises a VH domain comprising the sequence of SEQ ID NO:143 and a VL domain comprising the sequence of SEQ ID NO:144.

109. The multispecific binding molecule of any one of claims 71-98, wherein one or both of the first and second antibodies or fragments are human or humanized antibodies or fragments.

110. The multispecific binding molecule of any one of claims 71-109, wherein one or both of the first and second antibodies or fragments are Fab, Fab', F(ab')2, Fv, Fab'-SH, F(ab')2, single chain antibodies, nanobodies, or scFv fragments.

111. The multispecific binding molecule of any one of claims 71-109, wherein one or both of the first and second antibodies or fragments further comprise an Fc domain.

112. The multispecific binding molecule of any one of claims 71-109, wherein the first antibody or fragment is a Fab fragment, and wherein the second antibody comprises an antibody heavy chain and an antibody light chain.

113. The multispecific binding molecule of any one of claims 71-109, wherein the first and the second antibodies both comprise an antibody heavy chain and an antibody light chain.

114. The multispecific binding molecule of any one of claims 71-113, wherein the first antibody or fragment is coupled to avidin, streptavidin, neutravidin, or a biotin-binding derivative thereof, and the second antibody or fragment is coupled to biotin or an avidin-binding derivative thereof; or wherein the second antibody or fragment is coupled to avidin, streptavidin, neutravidin, or a biotin-binding derivative thereof, and the first antibody or fragment is coupled to biotin or an avidin-binding derivative thereof; and wherein the first antibody or fragment is bound to the second antibody or fragment via an interaction between the avidin, streptavidin, neutravidin, or biotin-binding derivative thereof and the biotin or avidin-binding derivative thereof.

115. The multispecific binding molecule of claim 114, wherein the first antibody or fragment is a Fab fragment coupled to monomeric streptavidin (mSA), and wherein the second antibody is a biotinylated antibody that comprises an antibody heavy chain and an antibody light chain.

116. The multispecific binding molecule of claim 114, wherein the first antibody or fragment is a full-length antibody coupled to monomeric streptavidin (mSA), and wherein the second antibody is a biotinylated antibody that comprises an antibody heavy chain and an antibody light chain.

117. The multispecific binding molecule of any one of claims 71-109, wherein the multispecific binding molecule comprises a first IgG antibody comprising the first antigen binding domain covalently linked to a second IgG antibody comprising the second antigen binding domain.

118. The multispecific binding molecule of any one of claims 71-109, wherein the multispecific binding molecule comprises a first antibody arm comprising a single chain variable fragment (scFv) comprising the VH and VL domains that bind to human Dectin-1 and a first Fc region, and a second antibody arm comprising an antibody heavy chain that comprises the VH domain of the second antigen binding domain in association with an antibody light chain that comprises the VL domain of the second antigen binding domain and a second Fc region connected to the VH domain of the second antigen binding domain.

119. The multispecific binding molecule of claim 118, wherein the first Fc region comprises one or more knob-forming mutations, and the second Fc region comprises one or more cognate hole-forming mutations, or wherein the second Fc region comprises one or more knob-forming mutations, and the first Fc region comprises one or more cognate hole-forming mutations.

120. The multispecific binding molecule of claim 118 or claim 119, wherein the first antibody arm comprises a first linker between the VH and VL domains, and a second linker between the VL domain and the first Fc region.

121. The multispecific binding molecule of claim 120, wherein the first linker comprises one or more repeats of the sequence GGGGS (SEQ ID NO:115).

122. The multispecific binding molecule of claim 121, wherein the first linker comprises the sequence GGGGSGGGGSGGGGS (SEQ ID NO:116) or GGGGSGGGGSGGGGSGGGGS (SEQ ID NO:117).

123. The multispecific binding molecule of any one of claims 120-122, wherein the second linker comprises the sequence EPKRSDKTHTCPPC (SEQ ID NO:118) or SATHTCPPC (SEQ ID NO:119).

124. The multispecific binding molecule of any one of claims 120-123, wherein the VH domain of the first antibody arm comprises the amino acid sequence of SEQ ID NO:220, and wherein the VL domain of the first antibody arm comprises the amino acid sequence of SEQ ID NO:221.

125. The multispecific binding molecule of claim 124, wherein the scFv comprises the amino acid sequence of SEQ ID NO:222.

126. The multispecific binding molecule of claim 124, wherein the first antibody arm comprises the amino acid sequence of SEQ ID NO:224 or 225.

127. The multispecific binding molecule of any one of claims 71-109, wherein the multispecific binding molecule comprises a first antibody arm comprising a first antibody heavy chain that comprises the VH domain of the first antigen binding domain and a first Fc region and a first antibody light chain comprising the VL domain of the first antigen binding domain, and a second antibody arm comprising a second antibody heavy chain that comprises the VH domain of the second antigen binding domain and a second Fc region and a second antibody light chain comprising the VL domain of the second antigen binding domain, wherein the first Fc region comprises one or more knob-forming mutations, and the second Fc region comprises one or more cognate hole-forming mutations.

128. The multispecific binding molecule of claim 119 or claim 127, wherein the first Fc region comprises a T366W substitution, and wherein the second Fc region comprises T366S, L368A, and Y407V substitutions, according to EU numbering.

129. The multispecific binding molecule of any one of claims 71-109, wherein the multispecific binding molecule comprises a first antibody arm comprising a first antibody heavy chain that comprises the VH domain of the first antigen binding domain and a first Fc region, and a second antibody arm comprising a second antibody heavy chain that comprises the VH domain of the second antigen binding domain and a second Fc region, wherein the first Fc region comprises one or more hole-forming mutations, and the second Fc region comprises one or more cognate knob-forming mutations.

130. The multispecific binding molecule of claim 119 or claim 129, wherein the first Fc region comprises T366S, L368A, and Y407V substitutions, and wherein the second Fc region comprises a T366W substitution, according to EU numbering.

131. The multispecific binding molecule of any one of claims 127-130, wherein the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:209, and wherein the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:210.

132. The multispecific binding molecule of any one of claims 127-130, wherein the VH domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID

NO:220, and wherein the VL domain of the first antigen binding domain comprises the amino acid sequence of SEQ ID NO:221.

133. The multispecific binding molecule of claim 132, wherein the first antibody heavy chain comprises a C→S substitution at position 5, according to IMGT hinge numbering, and wherein the first antibody light chain comprises a C→S substitution at the terminal residue of the light chain constant domain.

134. The multispecific binding molecule of claim 132, wherein the first antibody heavy chain comprises the amino acid sequence of SEQ ID NO:219, and wherein the first antibody light chain comprises the amino acid sequence of SEQ ID NO:223.

135. The multispecific binding molecule of any one of claims 111-134, wherein one or both of the first and second antibodies or fragments comprise a human IgG Fc region.

136. The multispecific binding molecule of claim 135, wherein the Fc region is a human IgG1 or human IgG4 Fc region.

137. The multispecific binding molecule of claim 136, wherein the Fc region is:

(a) a human IgG1 Fc region comprising S239D and I332E substitutions, according to EU numbering;

(b) a human IgG1 Fc region comprising S239D, A330L, and I332E substitutions, according to EU numbering;

(c) a human IgG1 Fc region comprising G236A, S239D, A330L, and I332E substitutions, according to EU numbering; or

(d) a human IgG4 Fc region comprising an S228P substitution, according to EU numbering.

138. The multispecific binding molecule of claim 136, wherein the multispecific binding molecule comprises two antibody heavy chains, and wherein each of the antibody heavy chains comprises an amino acid substitution at one or more of positions 234, 235, and 237, according to EU numbering.

139. The multispecific binding molecule of claim 138, wherein each of the antibody heavy chains comprises L234A, L235E, and G237A substitutions, according to EU numbering.

140. The multispecific binding molecule of any one of claims 136-139, wherein the multispecific binding molecule comprises two antibody heavy chains, and wherein only one of the antibody heavy chains comprises H435R and Y436F substitutions, according to EU numbering.

141. The multispecific binding molecule of any one of claims 111-140, wherein only one of the antibody arms comprises a heavy chain comprising F126C and C220V substitutions and a light chain comprising S121C and C214V substitutions, according to EU numbering.

142. The multispecific binding molecule of any one of claims 71-109, wherein the multispecific binding molecule comprises a first antibody heavy chain and a first antibody light chain and a second antibody heavy chain and a second antibody light chain, wherein the VH domain of the first antibody heavy chain forms a first antigen binding domain with the VL domain of the first antibody light chain, wherein the VH domain of the second antibody heavy chain forms a second antigen binding domain with the VL domain of the second antibody light chain, wherein the first antibody heavy chain comprises F126C, C220V, and T366W substitutions, wherein the first antibody light chain comprises S121C and C214V substitutions, and wherein the second antibody heavy chain comprises T366S, L368A, Y407V, H435R, and Y436F substitutions, according to EU numbering.

143. The multispecific binding molecule of claim 142, wherein the first and second antibody heavy chains further comprise L234A, L235E, and G237A substitutions, according to EU numbering.

144. The multispecific binding molecule of any one of claims 111-143, wherein at least one or two of the first and second antibody heavy chains is/are non-fucosylated or comprise(s) reduced fucosylation.

145. A multispecific binding molecule, comprising:

(a) a first arm comprising a single chain variable fragment (scFv) that binds to human Dectin-1 and a first Fc region, wherein the scFv comprises a first VH domain and a first VL domain, and

(b) a second arm that comprises a second antibody comprising a second antigen binding domain and a second Fc region, wherein the second antigen binding domain binds to a target of interest;

wherein the VH domain of the first antibody arm comprises the amino acid sequence of SEQ ID NO:220, and wherein the VL domain of the first antibody arm comprises the amino acid sequence of SEQ ID NO:221.

146. The multispecific binding molecule of claim 145, wherein the scFv comprises the amino acid sequence of SEQ ID NO:222.

147. The multispecific binding molecule of claim 145, wherein the first arm comprises the amino acid sequence of SEQ ID NO:224 or 225.

148. A multispecific binding molecule, comprising:

(a) a first arm comprising a first antibody heavy chain and a first antibody light chain, wherein the first antibody heavy chain comprises a first VH domain and a first Fc region, wherein the first antibody light chain comprises a first VL domain, and wherein the first VH and VL domains form a first antigen binding domain that binds to human Dectin-1; and

(b) a second arm comprising a second antibody heavy chain and a second antibody light chain, wherein the second antibody heavy chain comprises a second VH domain and a second Fc region, wherein the second antibody light chain comprises a second VL domain, and wherein the second VH and VL domains form a second antigen binding domain that binds to a target of interest;

wherein:

the first VH domain comprises the amino acid sequence of SEQ ID NO:209 and the first VL domain comprises the amino acid sequence of SEQ ID NO:210, or

the first VH domain comprises the amino acid sequence of SEQ ID NO:220 and the first VL domain comprises the amino acid sequence of SEQ ID NO:221.

149. The multispecific binding molecule of claim 148, wherein the first antibody heavy chain comprises a C→S substitution at position 5, according to IMGT hinge numbering, and wherein

the first antibody light chain comprises a C→S substitution at the terminal residue of the light chain constant domain.

150. The multispecific binding molecule of claim 148, wherein the first antibody heavy chain comprises the amino acid sequence of SEQ ID NO:219, and wherein the first antibody light chain comprises the amino acid sequence of SEQ ID NO:223.

151. A polynucleotide encoding the antibody or multispecific binding molecule of any one of claims 1-150.

152. A vector comprising the polynucleotide of claim 151.

153. An isolated host cell comprising the polynucleotide of claim 151 or the vector of claim 152.

154. The isolated host cell of claim 153, wherein the host cell is a yeast, insect, plant, or prokaryotic cell.

155. The isolated host cell of claim 153, wherein the host cell is a mammalian cell.

156. The isolated host cell of claim 155, wherein the mammalian cell is a Chinese hamster ovary (CHO) cell.

157. The isolated host cell of claim 155 or claim 156, wherein the host cell comprises an alpha1,6-fucosyltransferase (Fut8) or alpha-1,3-mannosyl-glycoprotein 2-beta-N-acetylglucosaminyltranferase (MGAT1) knockout.

158. The isolated host cell of claim 155 or claim 156, wherein the host cell overexpresses β1,4-N-acetylglucosaminyltransferase III (GnT-III).

159. The isolated host cell of claim 158, wherein the host cell further overexpresses Golgi μ-mannosidase II (ManII).

160. A method of producing an antibody or multispecific binding molecule, comprising culturing the host cell of any one of claims 153-159 under conditions suitable for production of the antibody or multispecific binding molecule.

161. The method of claim 160, further comprising recovering the antibody or multispecific binding molecule.

162. The method of claim 160 or claim 161, wherein, prior to production of the antibody or multispecific binding molecule, the host cell is treated with kifunensine.

163. An antibody or antigen-binding fragment thereof that binds to human Dectin-1 produced by the method of any one of claims 160-162.

164. A pharmaceutical composition comprising the antibody or multispecific binding molecule of any one of claims 1-150 and 163 and a pharmaceutically acceptable carrier.

165. A method of treating a disease or disorder, comprising administering an effective amount of the antibody of any one of claims 1-70, the multispecific binding molecule of any one of claims 71-150, or the composition of claim 164 to an individual in need thereof.

166. The method of claim 165, wherein the first target of interest is human Dectin-1, and wherein the second target of interest is a disease-causing agent.

167. The method of claim 166, wherein the disease-causing agent is a bacterial cell, fungal cell, virus, senescent cell, tumor cell, protein aggregate, LDL particle, mast cell, eosinophil, ILC2 cell, or inflammatory immune cell.

168. The method of claim 167, wherein the target of interest is an antigen expressed on the surface of the bacterial cell, fungal cell, senescent cell, tumor cell, mast cell, eosinophil, ILC2 cell, or inflammatory immune cell.

169. The method of claim 167, wherein the target of interest is a surface antigen of the virus.

170. The method of any one of claims 165-169, wherein the disease or disorder is cancer, a bacterial infection, a fungal infection, a viral infection, a mast cell disease or disorder, systemic mastocytosis, amyloidosis, or an aging-related disease or disorder.

171. The method of any one of claims 165-170, wherein the target of interest is an antigen expressed on the surface of a cancer cell.

172. The method of claim 171, wherein the second target of interest is CD70, HER2, DLL3, NECTIN-4, TROP-2, Mesothelin, LIV-1, C-MET, FOLR1, CD20, CCR8, CD33, or EGFR.

173. A method of treating cancer, comprising administering an effective amount of a composition comprising the multispecific binding molecule of any one of claims 71-150, wherein the multispecific binding molecule comprises:

(a) a first antibody or antigen-binding fragment thereof comprising the first antigen-binding domain that binds to human Dectin-1; and

(b) a second antibody or antigen-binding fragment thereof comprising the second antigen-binding domain, wherein the second antigen binding domain binds to CD70, HER2, DLL3, NECTIN-4, TROP-2, Mesothelin, LIV-1, C-MET, FOLR1, CD20, CCR8, CD33, or EGFR.

174. The method of claim 173, wherein the second antigen binding domain binds to CD20; wherein the second antigen-binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; and wherein the VH domain of the second antigen-binding domain comprises the sequence of SEQ ID NO:129 and/or wherein the VL domain of the second antigen-binding domain comprises the sequence of SEQ ID NO:130.

175. The method of claim 173, wherein the second antigen binding domain binds to Trop-2; wherein the second antigen-binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; and wherein the VH domain of the second antigen-binding domain comprises the sequence of SEQ ID NO:139 and/or wherein the VL domain of the second antigen-binding domain comprises the sequence of SEQ ID NO:140.

176. The method of claim 173, wherein the second antigen binding domain binds to light chain amyloid; wherein the second antigen-binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; and wherein the VH domain of the second antigen-binding domain comprises the sequence of SEQ ID NO:143 and/or wherein the VL domain of the second antigen-binding domain comprises the sequence of (SEQ ID NO:144.

177. The method of any one of claims 173-176,

(a) the multispecific antibody comprises a first antibody arm comprising the first antigen binding domain and a first Fc region and a second antibody arm comprising the second antigen binding domain and a second Fc region, wherein the first Fc region comprises one or more knob-forming mutations, and the second Fc region comprises one or more cognate hole-forming mutations; or

(b) the multispecific antibody comprises a first antibody arm comprising the first antigen binding domain and a first Fc region and a second antibody arm comprising the second antigen binding domain and a second Fc region, wherein the first Fc region comprises one or more hole-forming mutations, and the second Fc region comprises one or more cognate knob-forming mutations.

178. The method of claim 177, wherein:

(a) wherein the first Fc region comprises a T366W substitution, and wherein the second Fc region comprises T366S, L368A, and Y407V substitutions, according to EU numbering; or

(b) the first Fc region comprises T366S, L368A, and Y407V substitutions, and wherein the second Fc region comprises a T366W substitution, according to EU numbering.

179. The method of any one of claims 173-178, wherein the antibody comprises two antibody heavy chains, and wherein only one of the antibody heavy chains comprises H435R and Y436F substitutions, according to EU numbering.

180. The method of any one of claims 173-179, wherein only one of the antibody arms comprises a heavy chain comprising F126C and C220V substitutions and a light chain comprising S121C and C214V substitutions, according to EU numbering.

181. The method of any one of claims 173-180, wherein the first and second antibody heavy chains comprise human IgG1 Fc domains.

182. The method of any one of claims 173-181, wherein at least one or two of the first and second antibody heavy chains is/are non-fucosylated or comprise(s) reduced fucosylation.

183. The method of any one of claims 173-182, wherein the individual is a human.

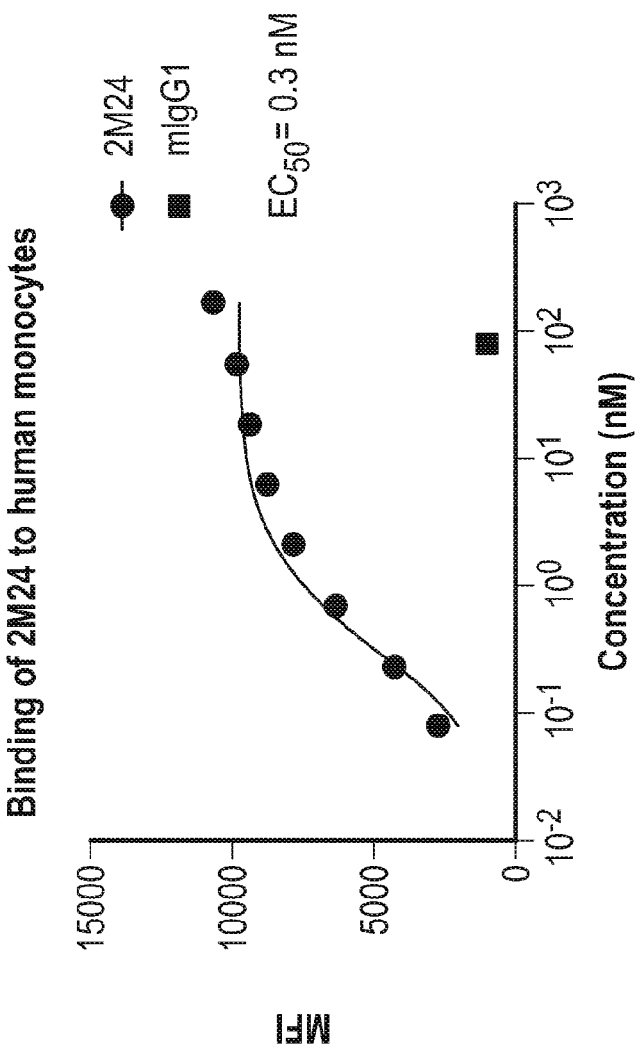

Binding of 2M24 to human monocytes
2M24
mIgG1
EC50= 0.3 nM
MFI
15000
10000
5000
0
10-2
10-1
100
101
102
103
Concentration (nM)

FIG. 1A

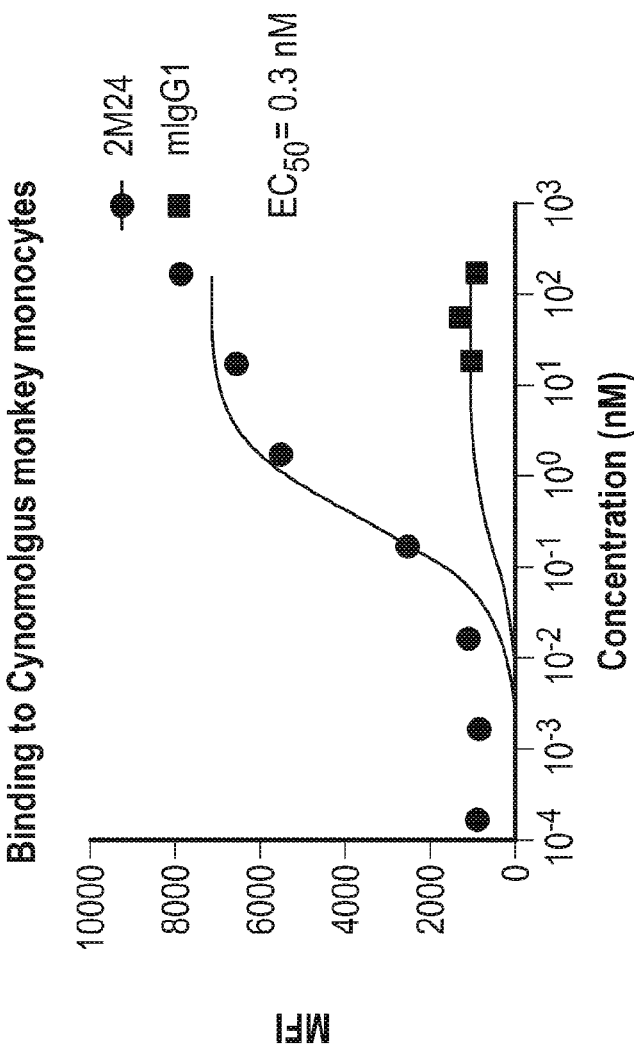

Binding to Cynomolgus monkey monocytes
2M24
mIgG1
EC50= 0.3 nM
MFI
10000
8000
6000
4000
2000
0
10-4
10-3
10-2
10-1
100
101
102
103
Concentration (nM)

FIG. 1B

Dectin-1 ab Clone	HEK-Blue hDectin-1a cells EC50 (nM)	HEK-Blue hDectin-1b cells EC50 (nM)	HEK293F hDectin-1a FL EC50 (nM))	Human monocytes EC50 (nM)	Cynomolgus monkey monocytes EC50 (nM)
2M24	0.4	1	1.1	0.3	0.3
2M08	2.6	>190	1.9	>190	N/A
2M12	16.9	>142	2.8	>142	N/A
2M38	4.5	>96	6.1	>96	N/A
2M49	>169	>169	>169	>169	N/A
15E2	1.2	9.3	1.4	0.6	14
259931	0.8	0.9	1.2	0.3	16.5
GE2	1.9	12	2.4	1.4	N/A

FIG. 1C

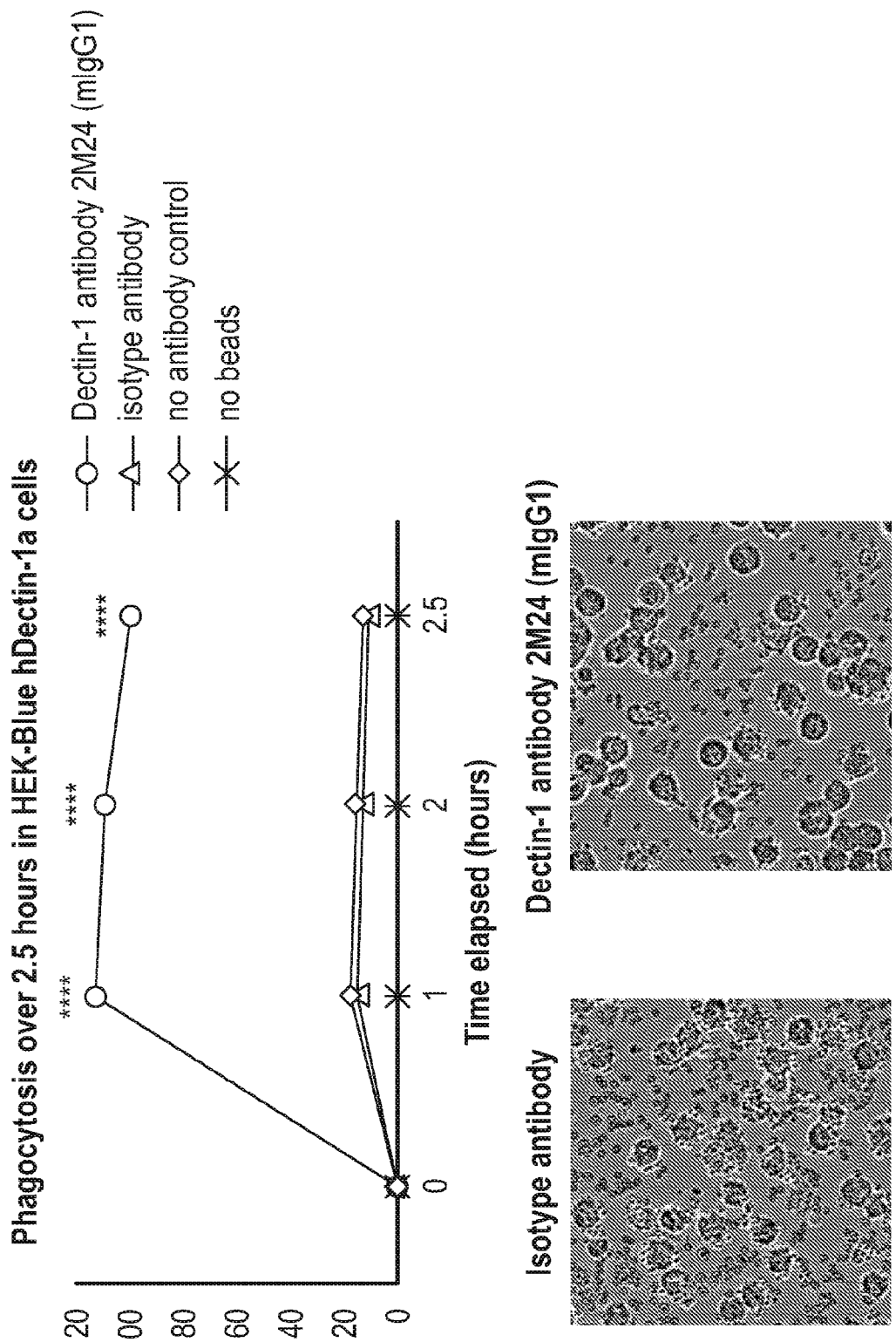

Phagocytosis over 2.5 hours in HEK-Blue hDectin-1a cells
Dectin-1 antibody 2M24 (mIgG1)
isotype antibody
no antibody control
no beads
****
****
****
Overlap (pHrod/calcein)/ green (calcein) object count
120
100
80
60
40
20
0
0
1
2
2.5
Time elapsed (hours)
Isotype antibody
Dectin-1 antibody 2M24 (mIgG1)

FIG. 2A

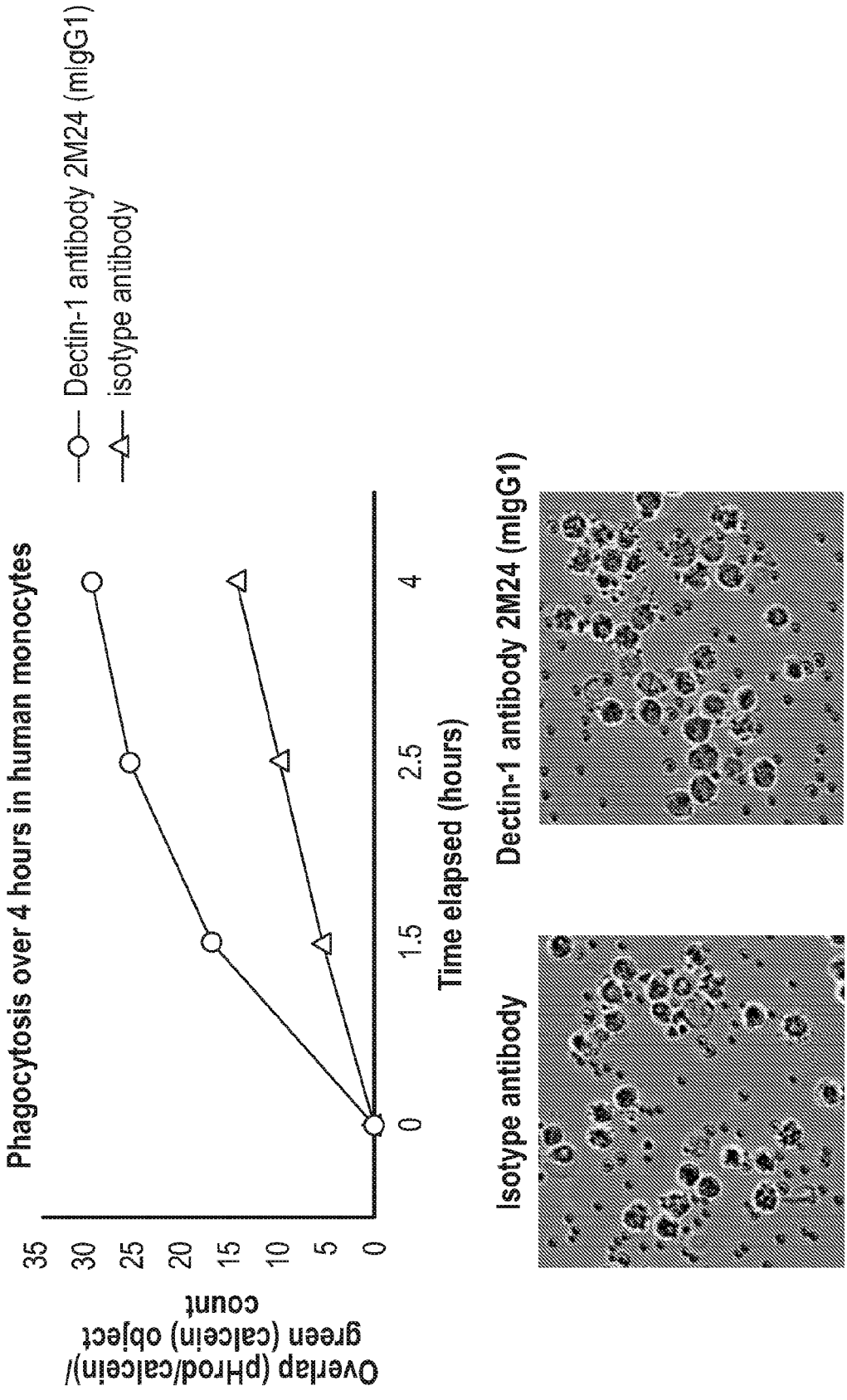

Phagocytosis over 4 hours in human monocytes
Dectin-1 antibody 2M24 (mIgG1)
isotype antibody
Overlap (pHrod/calcein)/ green (calcein) object count
35
30
25
20
15
10
5
0
0
1.5
2.5
4
Time elapsed (hours)
Isotype antibody
Dectin-1 antibody 2M24 (mIgG1)

FIG. 2B

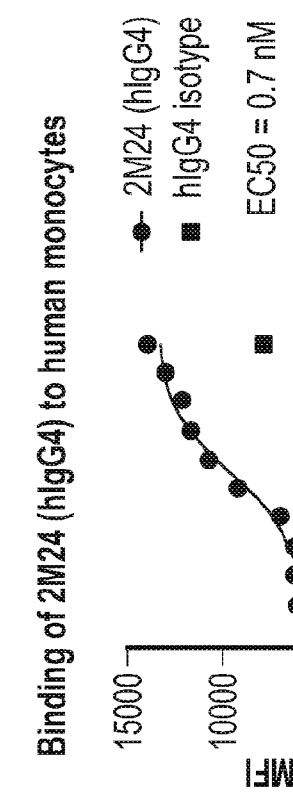

Binding of 2M24 (hIgG4) to human monocytes
MFI
15000
10000
5000
0
2M24 (hIgG4)
hIgG4 isotype
EC50 = 0.7 nM
10^{-2}
10^{0}
10^{2}
10^{4}
Concentration (nM)

FIG.3B

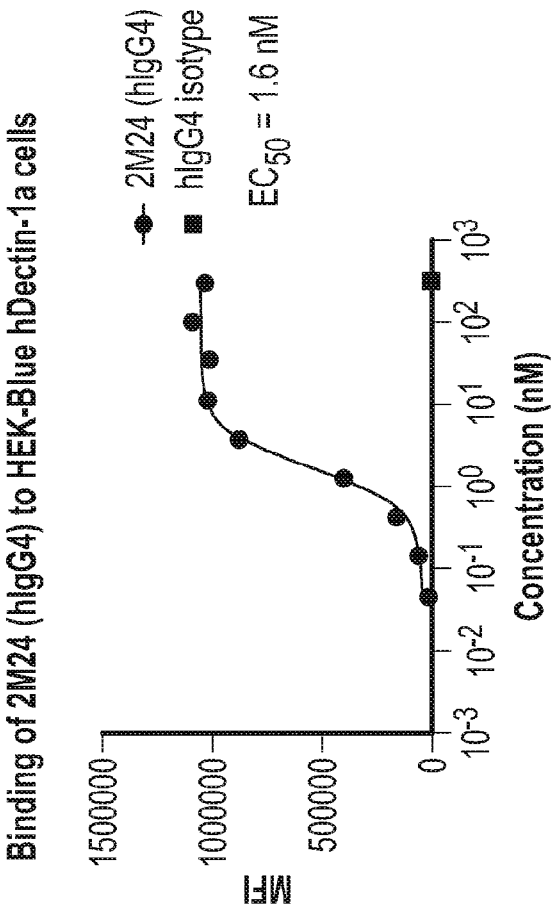

Binding of 2M24 (hIgG4) to HEK-Blue hDectin-1a cells
MFI
1500000
1000000
500000
0
2M24 (hIgG4)
hIgG4 isotype
EC_{50} = 1.6 nM
10^{-3}
10^{-2}
10^{-1}
10^{0}
10^{1}
10^{2}
10^{3}
Concentration (nM)

FIG.3A

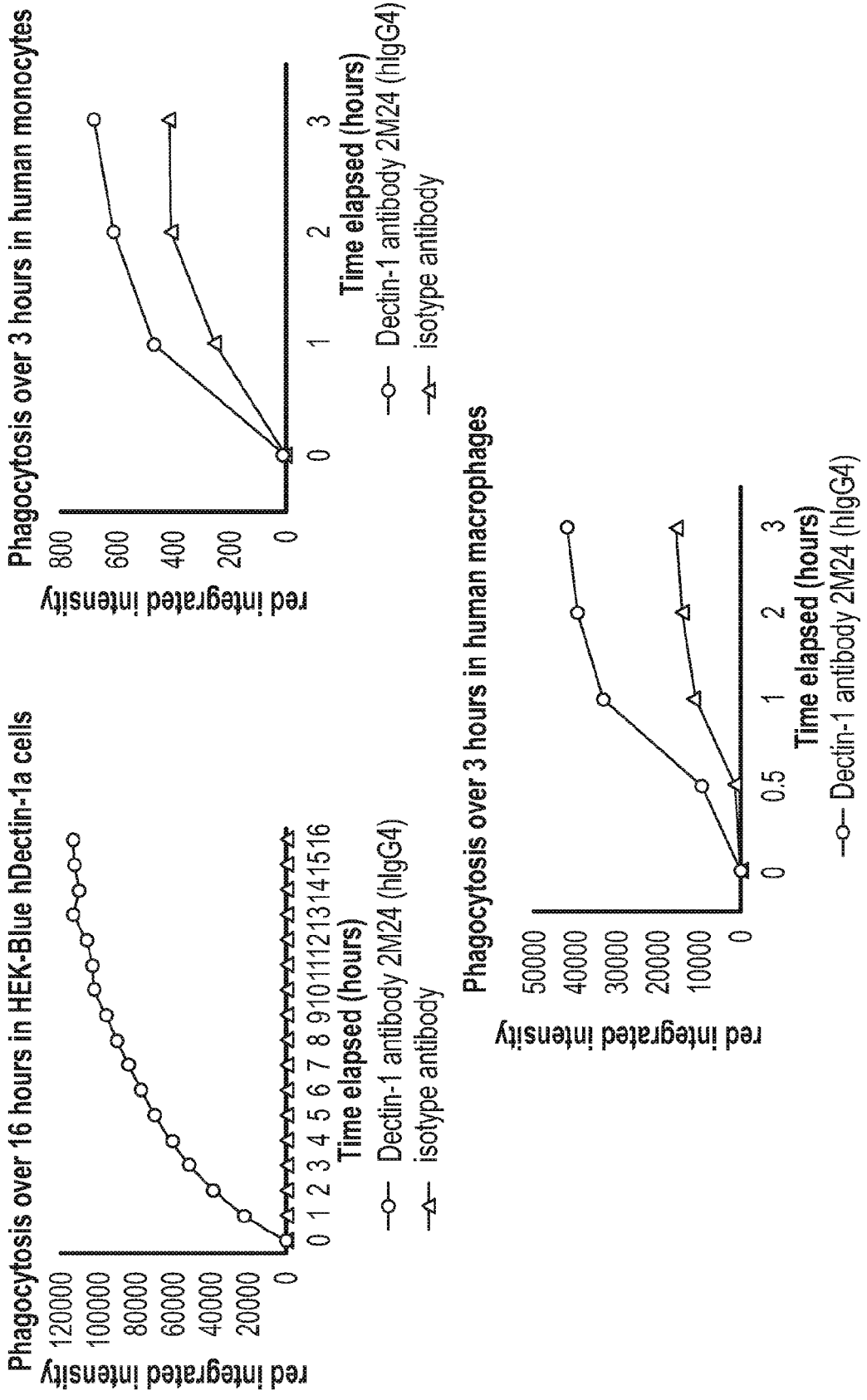

Phagocytosis over 16 hours in HEK-Blue hDectin-1a cells
red integrated intensity
120000
100000
80000
60000
40000
20000
0
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
Time elapsed (hours)
Dectin-1 antibody 2M24 (hIgG4)
isotype antibody
Phagocytosis over 3 hours in human monocytes
red integrated intensity
800
600
400
200
0
0 1 2 3
Time elapsed (hours)
Dectin-1 antibody 2M24 (hIgG4)
isotype antibody
Phagocytosis over 3 hours in human macrophages
red integrated intensity
50000
40000
30000
20000
10000
0
0 0.5 1 2 3
Time elapsed (hours)
Dectin-1 antibody 2M24 (hIgG4)
isotype antibody

FIG. 4

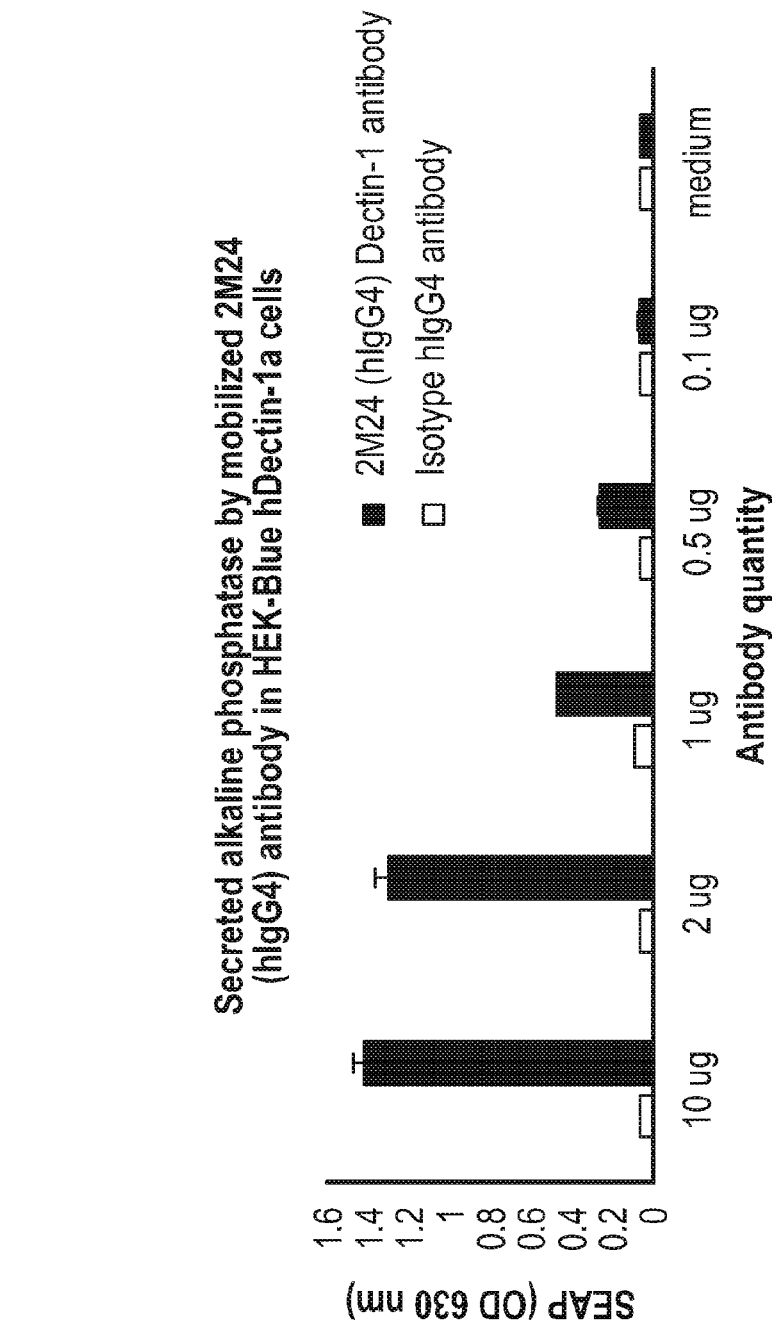

Secreted alkaline phosphatase by mobilized 2M24 (hIgG4) antibody in HEK-Blue hDectin-1a cells
2M24 (hIgG4) Dectin-1 antibody
Isotype hIgG4 antibody
SEAP (OD 630 nm)
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
10 ug
2 ug
1 ug
0.5 ug
0.1 ug
medium
Antibody quantity

FIG. 5A

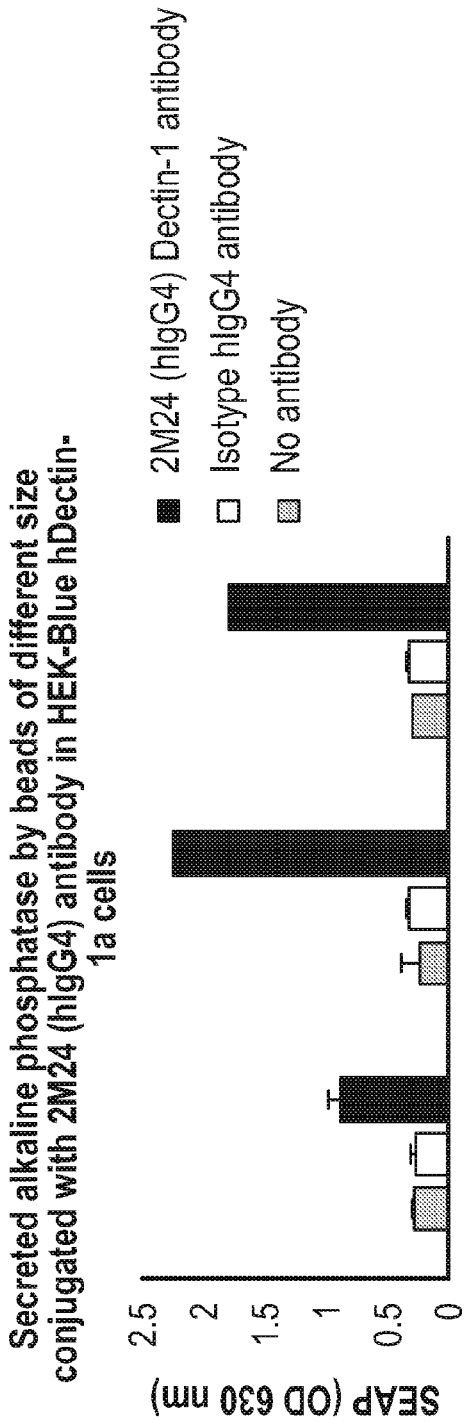

Secreted alkaline phosphatase by beads of different size conjugated with 2M24 (hIgG4) antibody in HEK-Blue hDectin-1a cells
SEAP (OD 630 nm)
2.5
2
1.5
1
0.5
0
3 µm
10 µm
16.5 µm
bead size
2M24 (hIgG4) Dectin-1 antibody
Isotype hIgG4 antibody
No antibody

FIG. 5B

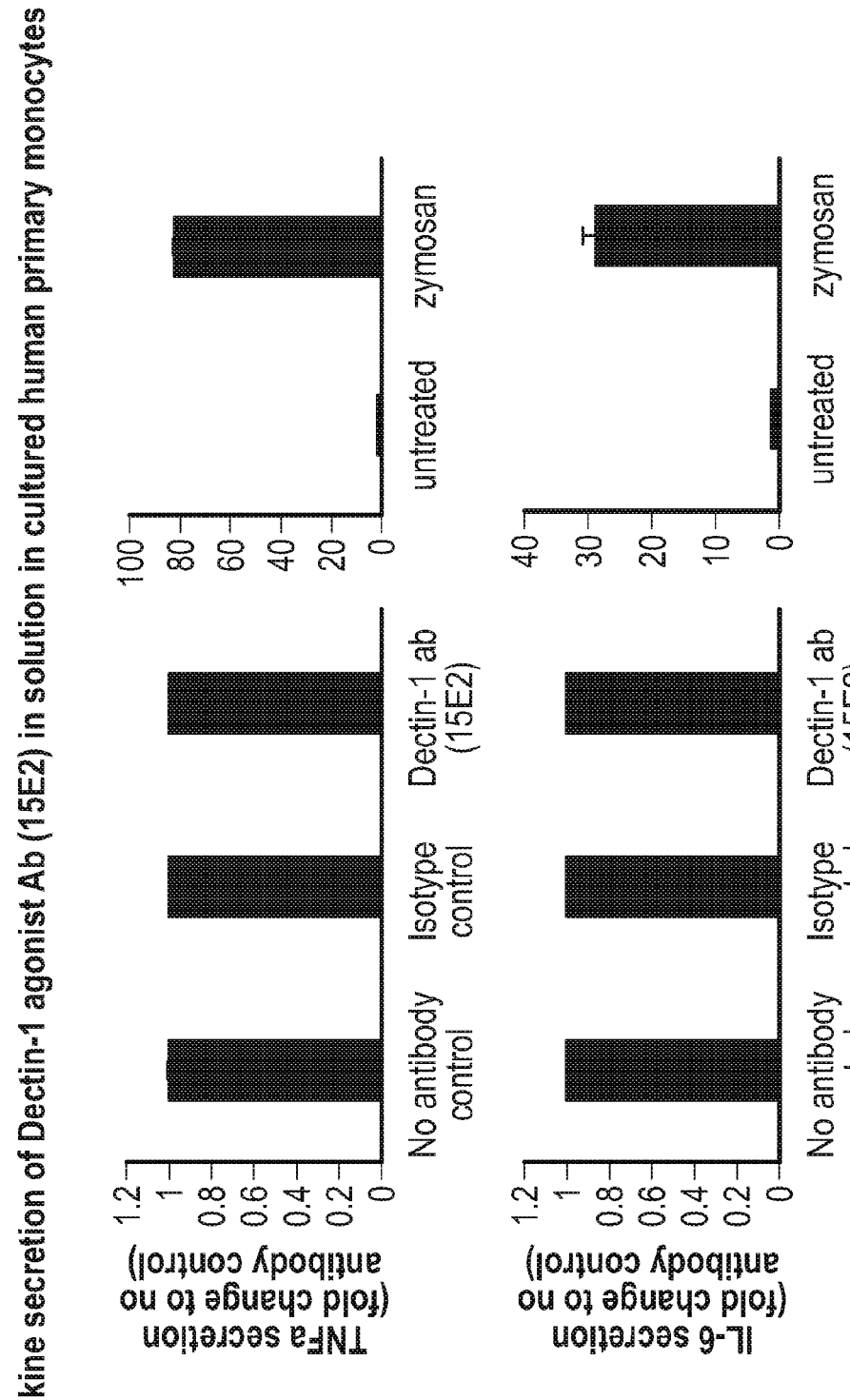

Cytokine secretion of Dectin-1 agonist Ab (15E2) in solution in cultured human primary monocytes
TNFa secretion (fold change to no antibody control)
1.2
1
0.8
0.6
0.4
0.2
0
No antibody control
Isotype control
Dectin-1 ab (15E2)
100
80
60
40
20
0
untreated
zymosan
IL-6 secretion (fold change to no antibody control)
1.2
1
0.8
0.6
0.4
0.2
0
No antibody control
Isotype control
Dectin-1 ab (15E2)
40
30
20
10
0
untreated
zymosan

FIG. 6A

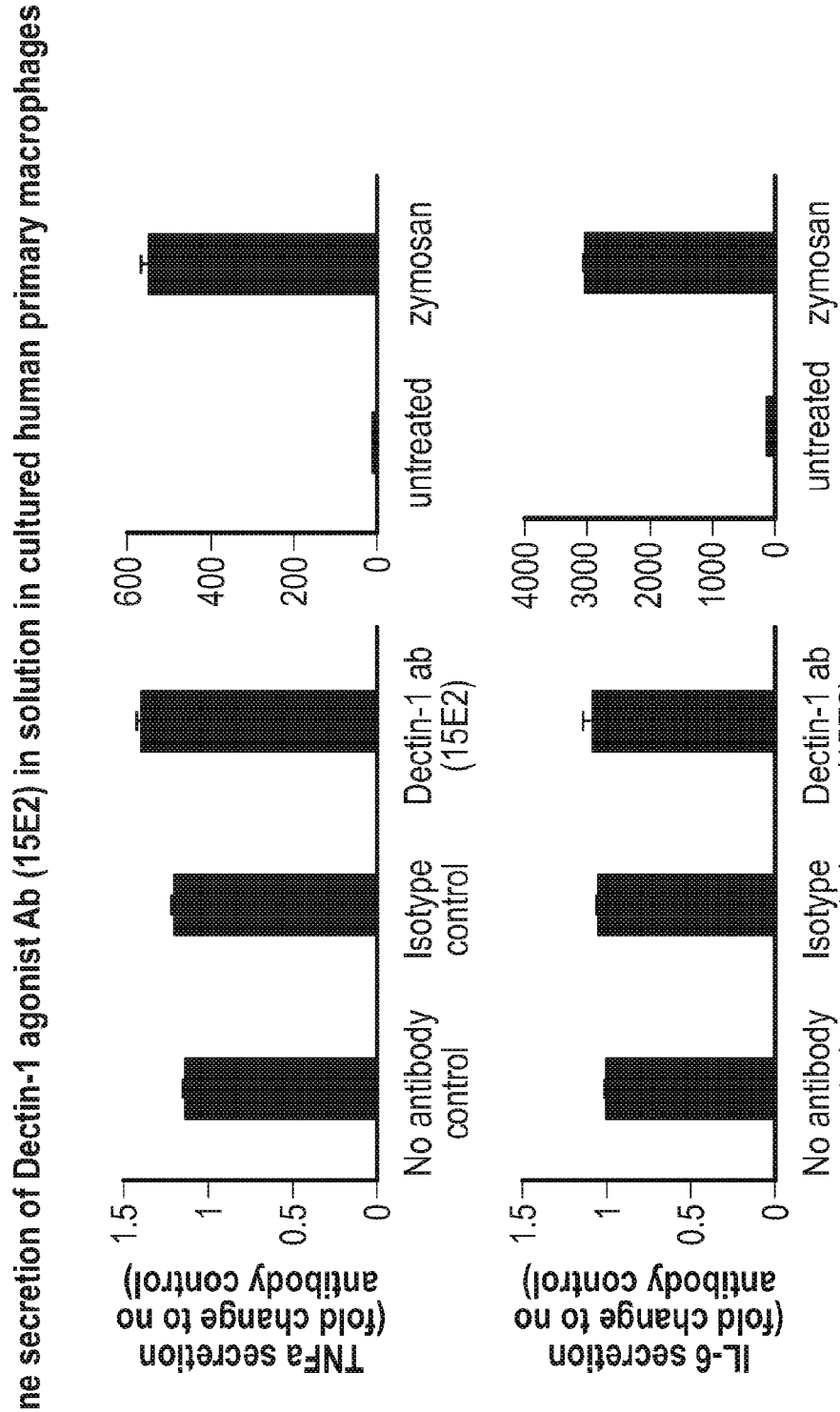

Cytokine secretion of Dectin-1 agonist Ab (15E2) in solution in cultured human primary macrophages
TNFa secretion (fold change to no antibody control)
1.5
1
0.5
0
No antibody control
Isotype control
Dectin-1 ab (15E2)
600
400
200
0
untreated
zymosan
IL-6 secretion (fold change to no antibody control)
4000
3000
2000
1000

FIG. 6B

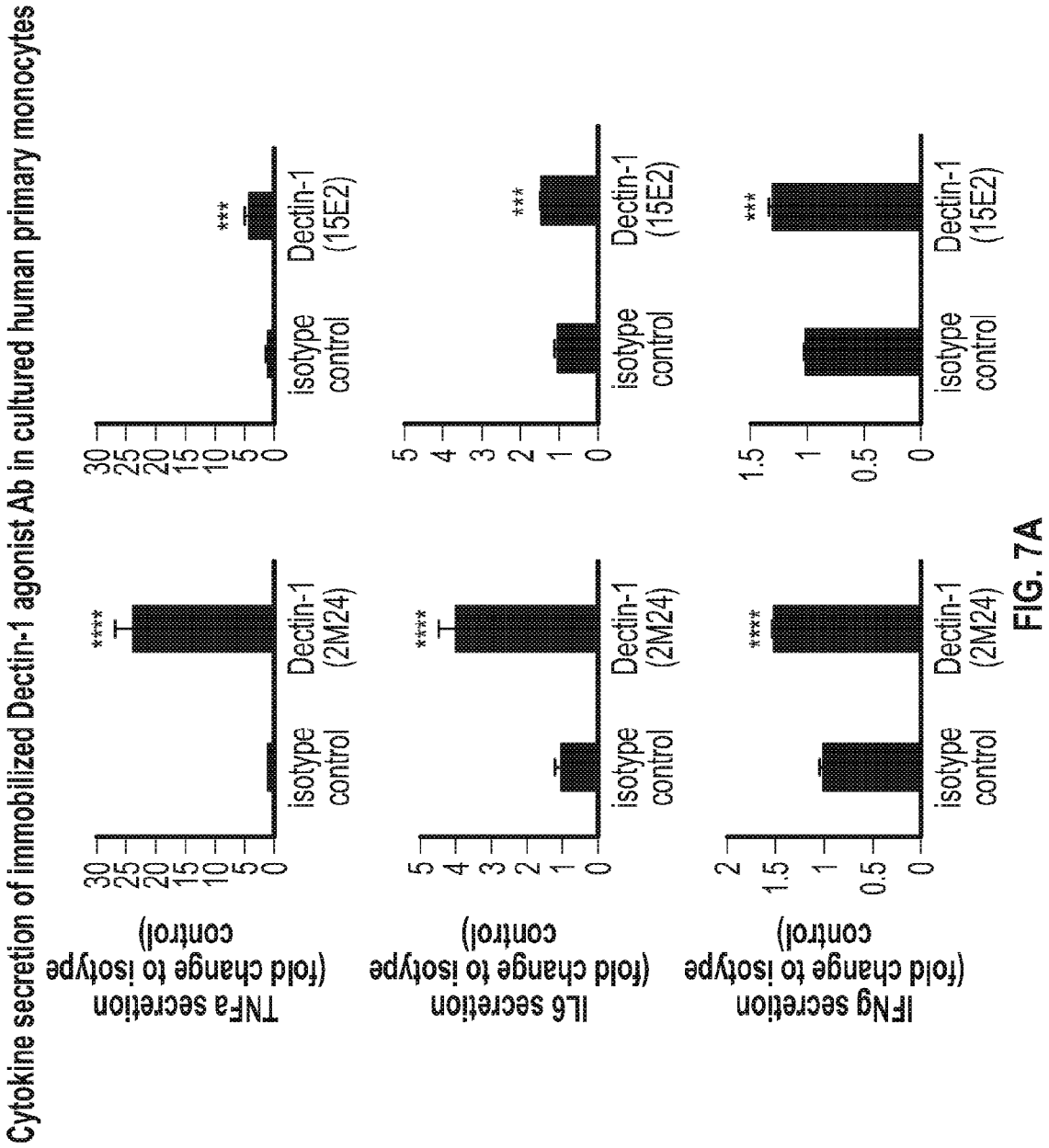

Cytokine secretion of immobilized Dectin-1 agonist Ab in cultured human primary monocytes
TNFa secretion (fold change to isotype control)
IL6 secretion (fold change to isotype control)
IFNg secretion (fold change to isotype control)
****
***
isotype control
Dectin-1 (2M24)
Dectin-1 (15E2)

FIG. 7A

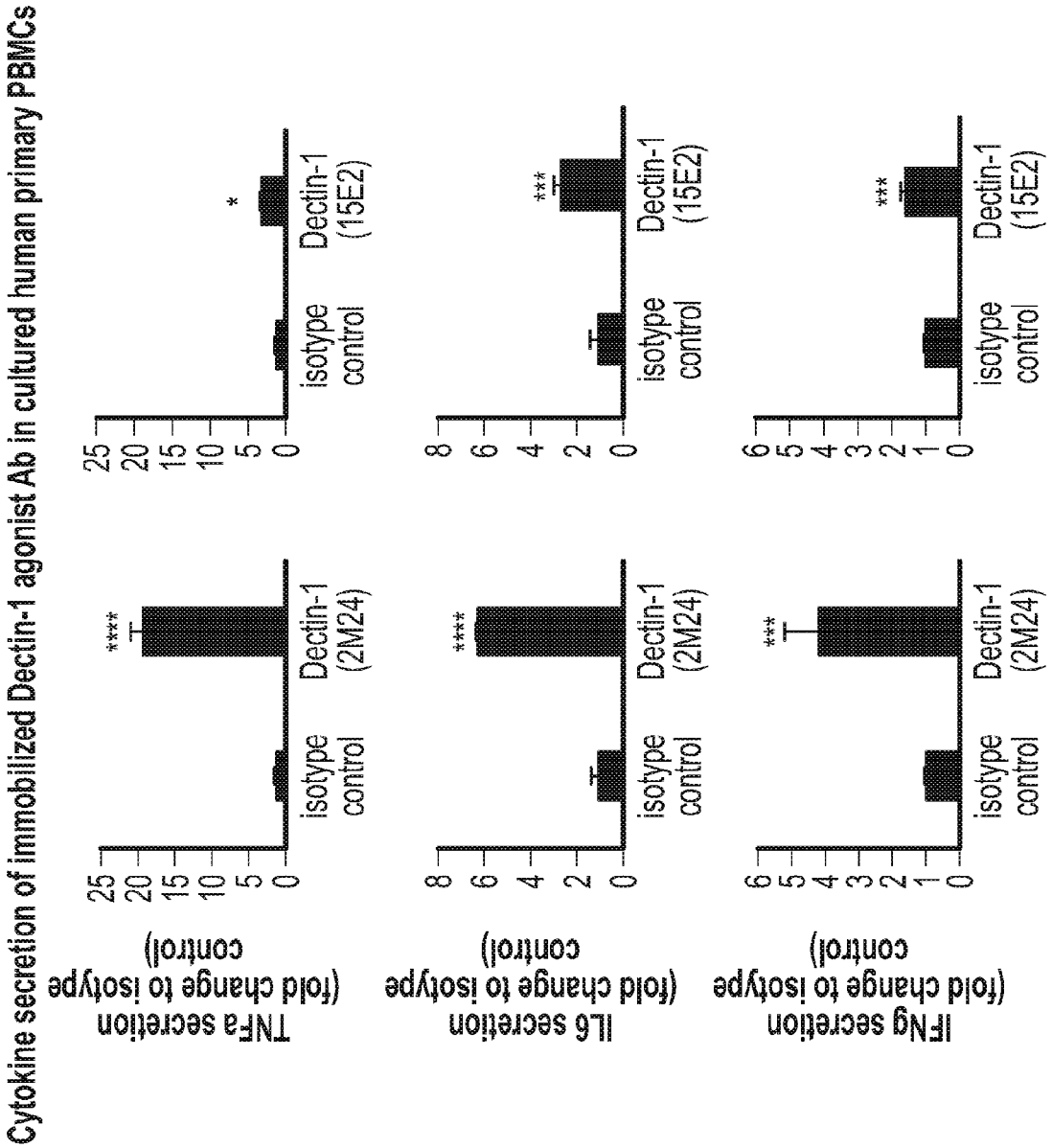

Cytokine secretion of immobilized Dectin-1 agonist Ab in cultured human primary PBMCs
TNFa secretion (fold change to isotype control)
IL6 secretion (fold change to isotype control)
IFNg secretion (fold change to isotype control)
isotype control
Dectin-1 (2M24)
Dectin-1 (15E2)
****
***
*

FIG. 7B

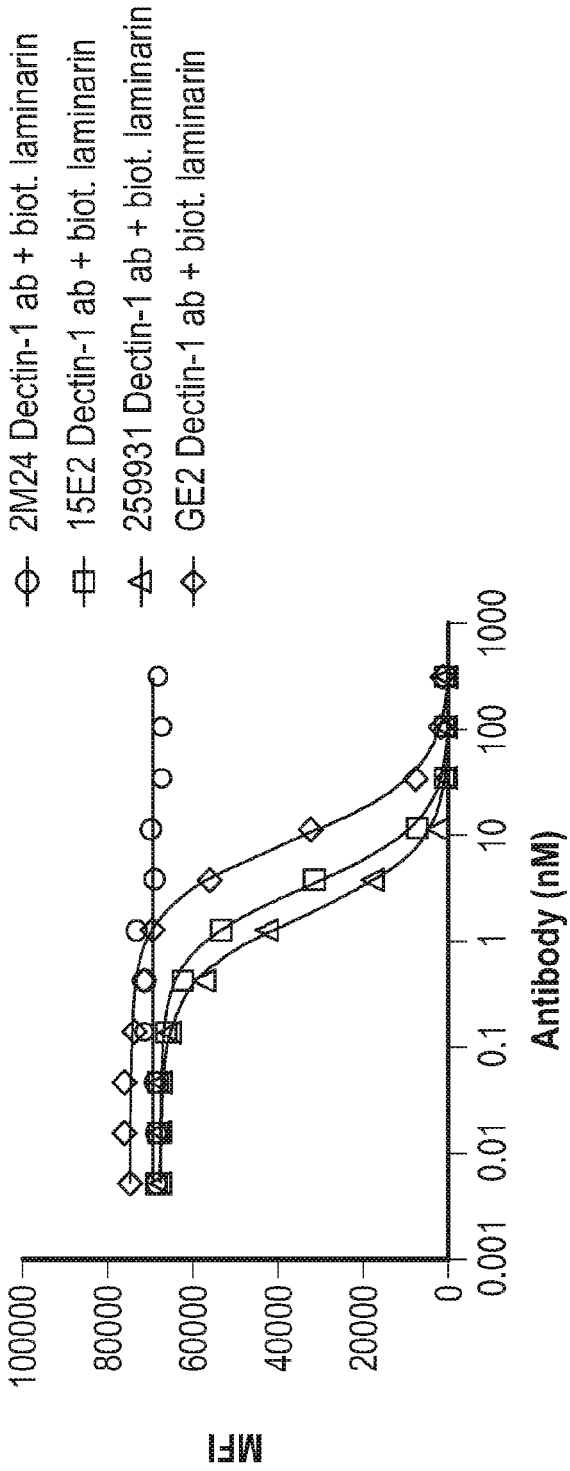

2M24 Dectin-1 ab + biot. laminarin
15E2 Dectin-1 ab + biot. laminarin
259931 Dectin-1 ab + biot. laminarin
GE2 Dectin-1 ab + biot. laminarin
MFI
100000
80000
60000
40000
20000
0
0.001
0.01
0.1
1
10
100
1000
Antibody (nM)

FIG. 8

Dectin-1 antibody Clone	HEK-Blue hDectin-1a cells EC50 (nM)	HEK-Blue hDectin-1b cells EC50 (nM)	HEK293F hDectin-1a FL EC50 (nM))	Human monocytes EC50 (nM)	Competition with natural ligands	TNFa secretion in PBMC (fold change to isotype)	IL6 secretion in PBMC (fold change to isotype)	IFNg secretion in PBMC (fold change to isotype)	Phagocytosis
2M24	0.4	1	1.1	0.3	NO	19	6.4	4.1	YES
15E2	1.2	9.3	1.4	0.6	YES	3	2.6	1.6	YES

FIG. 9

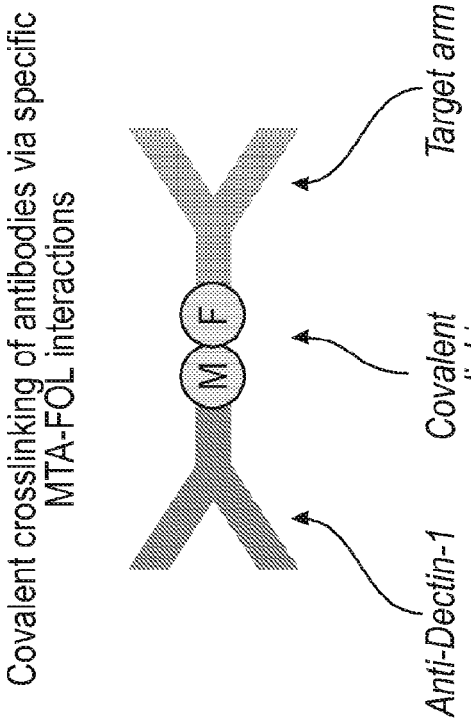


FIG. 10B

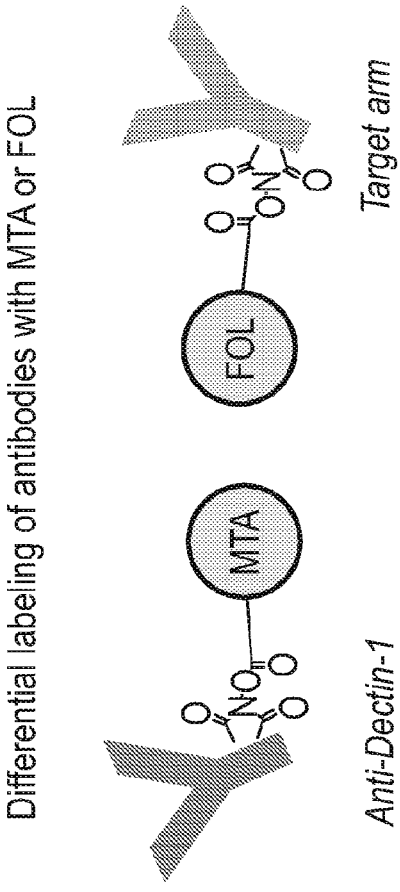


FIG. 10A

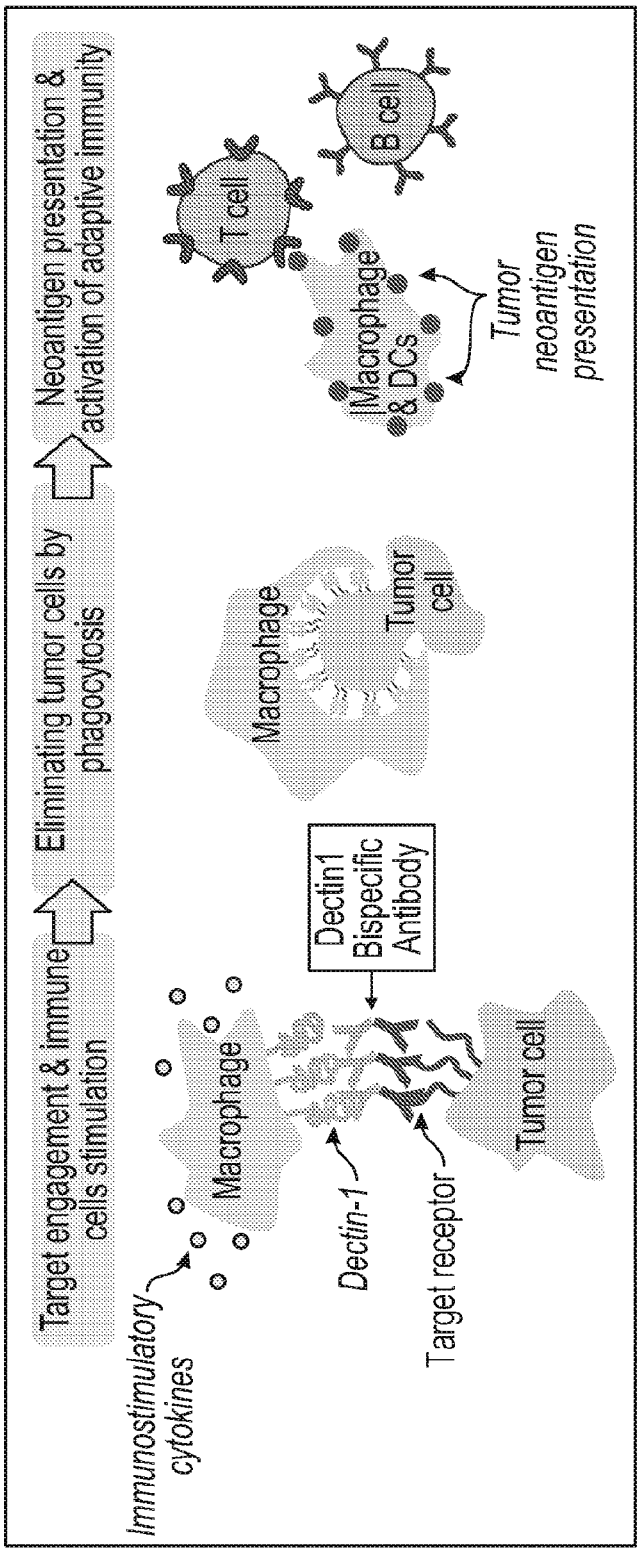


FIG. 11A

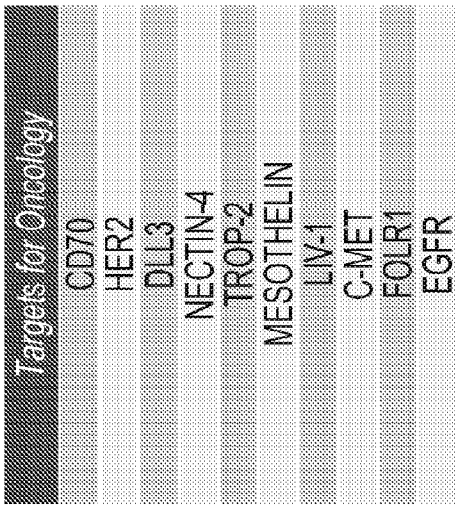


FIG. 11B

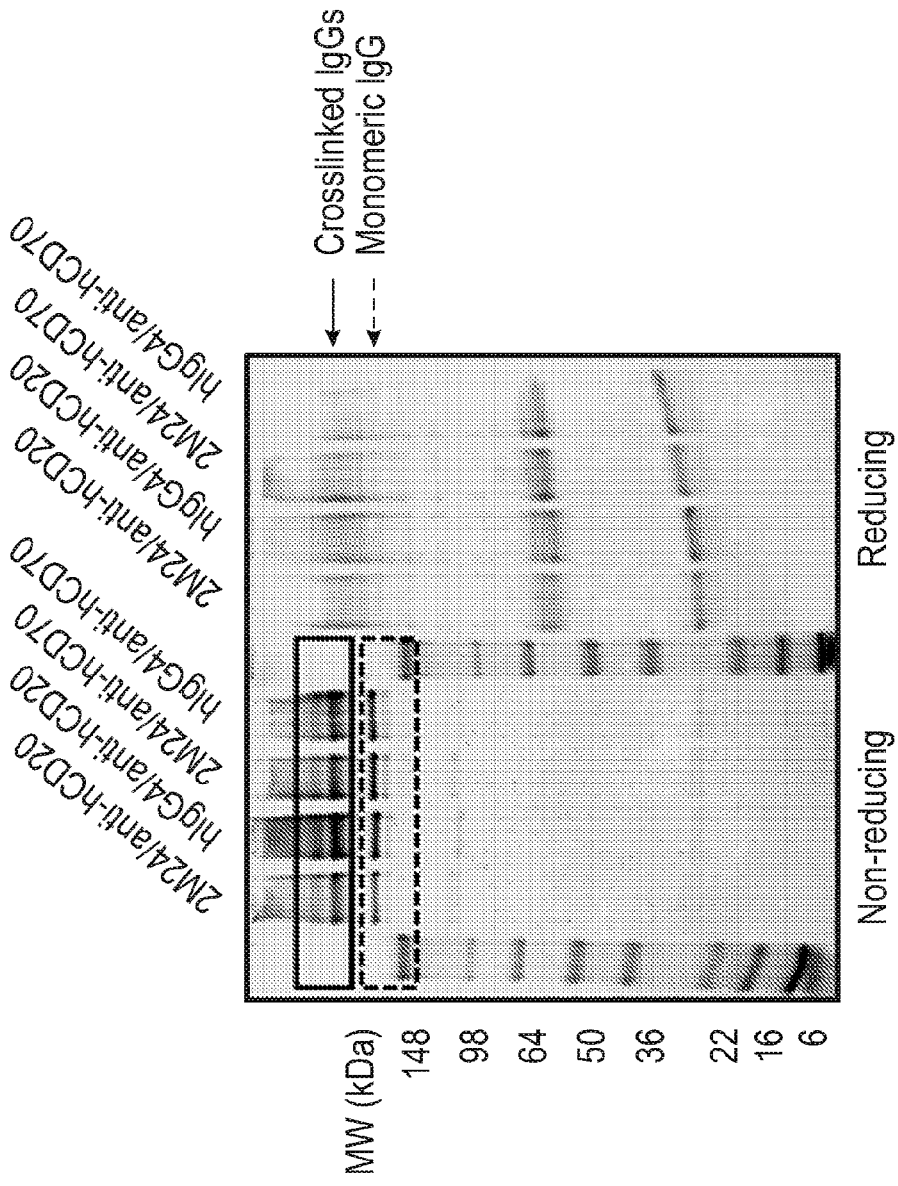
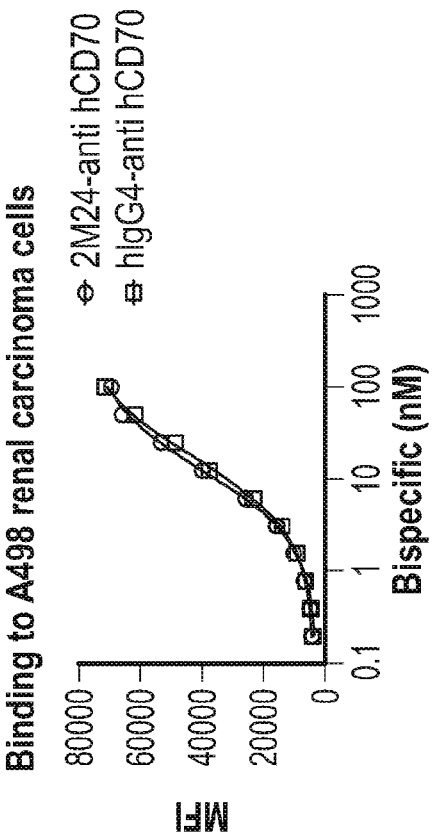
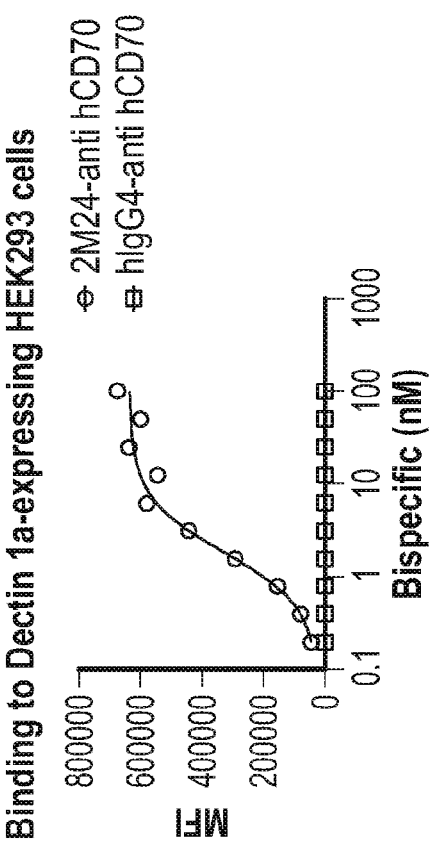

Crosslinked IgGs
Monomeric IgG
hIgG4/anti-hCD70
2M24/anti-hCD20
hIgG4/anti-hCD20
2M24/anti-hCD70
hIgG4/anti-hCD70
2M24/anti-hCD20
hIgG4/anti-hCD20
2M24/anti-hCD70
MW (kDa)
148
98
64
50
36
22
16
6
Non-reducing
Reducing

FIG. 12A





EC50 concentration (nM) of 2M24/anti-hCD70 bispecific binding to cell lines	
Dectin-1 expressing HEK293 cell line	1.8nM
A498 cell line	12.34 nM
786-0 cell line	11.62 nM

FIG. 12B

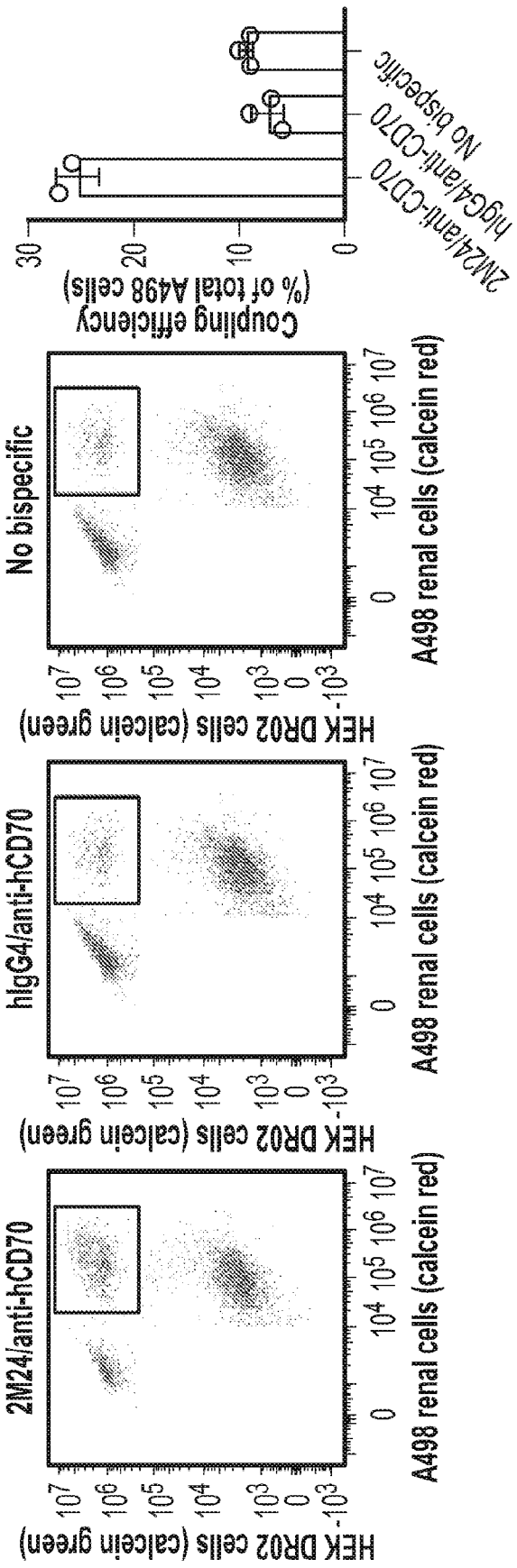

2M24/anti-hCD70
hIgG4/anti-hCD70
No bispecific
HEK DR02 cells (calcein green)
A498 renal cells (calcein red)
Coupling efficiency
(% of total A498 cells)
2M24/anti-CD70
hIgG4/anti-CD70
No bispecific

FIG. 13

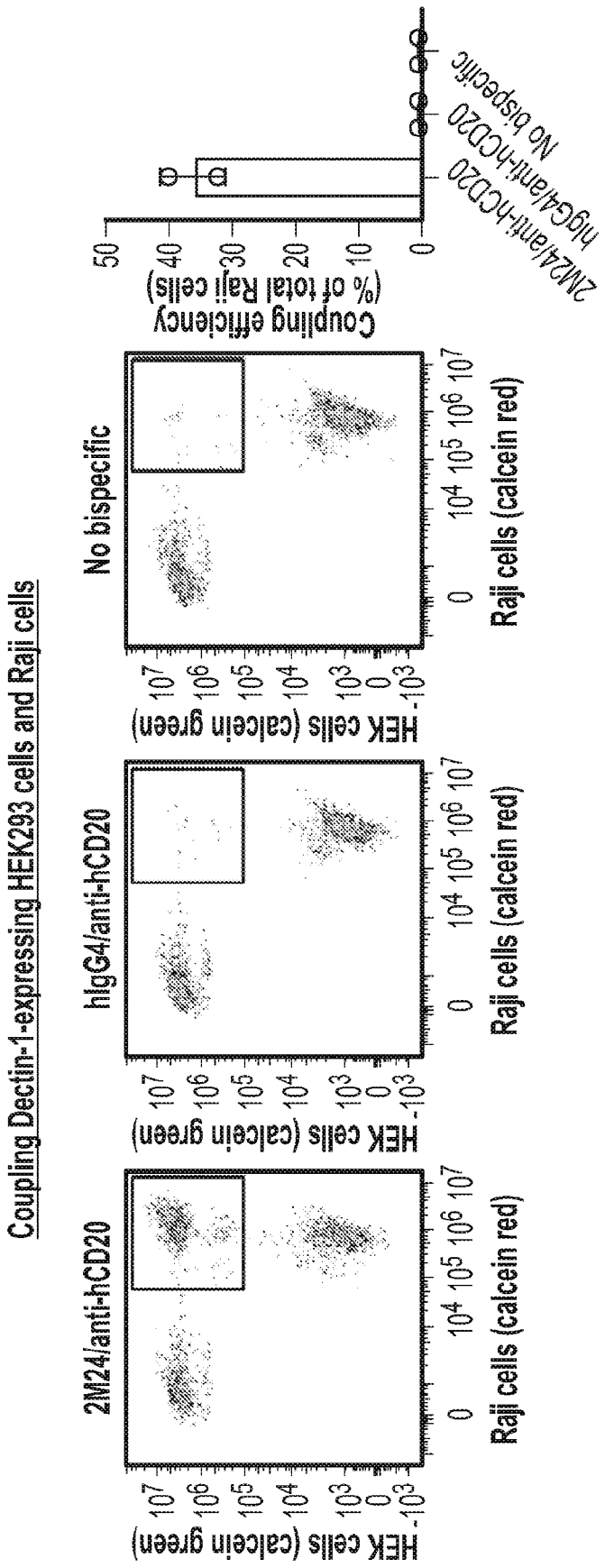

Coupling Dectin-1-expressing HEK293 cells and Raji cells
2M24/anti-hCD20
hIgG4/anti-hCD20
No bispecific
HEK cells (calcein green)
Raji cells (calcein red)
Coupling efficiency
(% of total Raji cells)
2M24/anti-hCD20
hIgG4/anti-hCD20
No bispecific

FIG. 14A

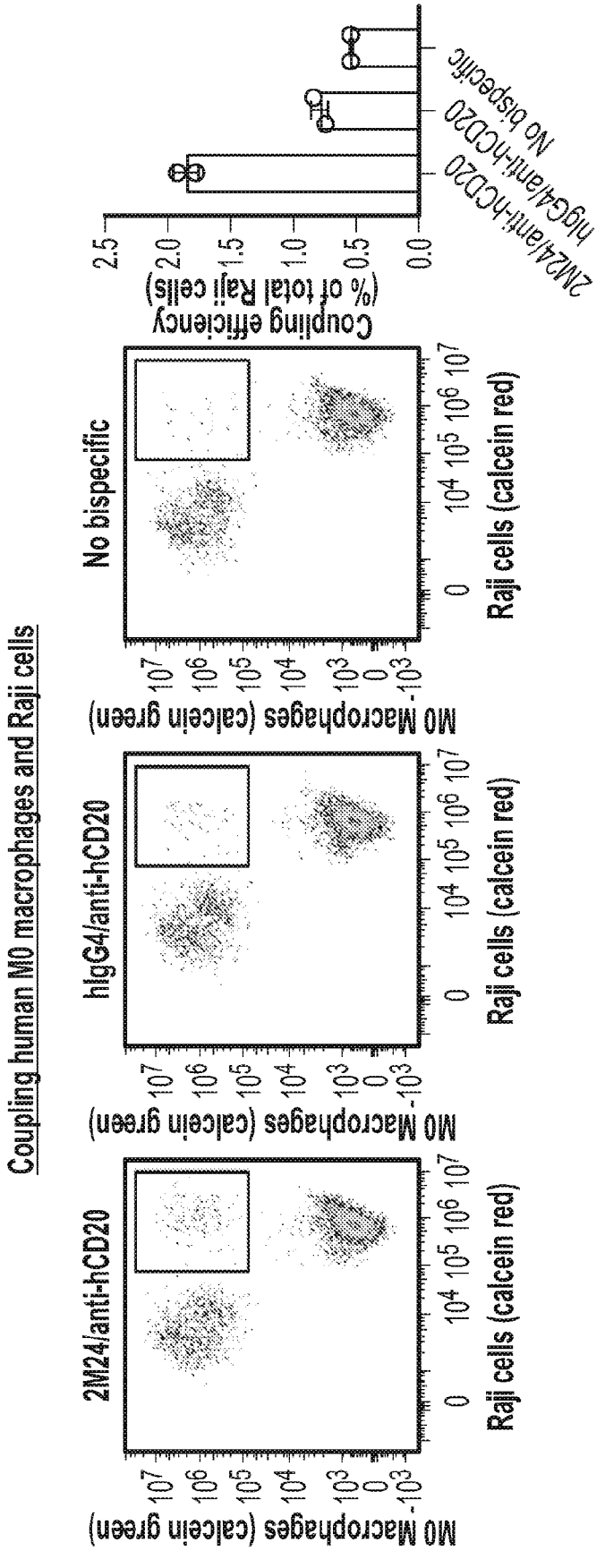

Coupling human M0 macrophages and Raji cells
2M24/anti-hCD20
hIgG4/anti-hCD20
No bispecific
M0 Macrophages (calcein green)
Raji cells (calcein red)
Coupling efficiency
(% of total Raji cells)
2M24/anti-hCD20
hIgG4/anti-hCD20
No bispecific

FIG. 14B

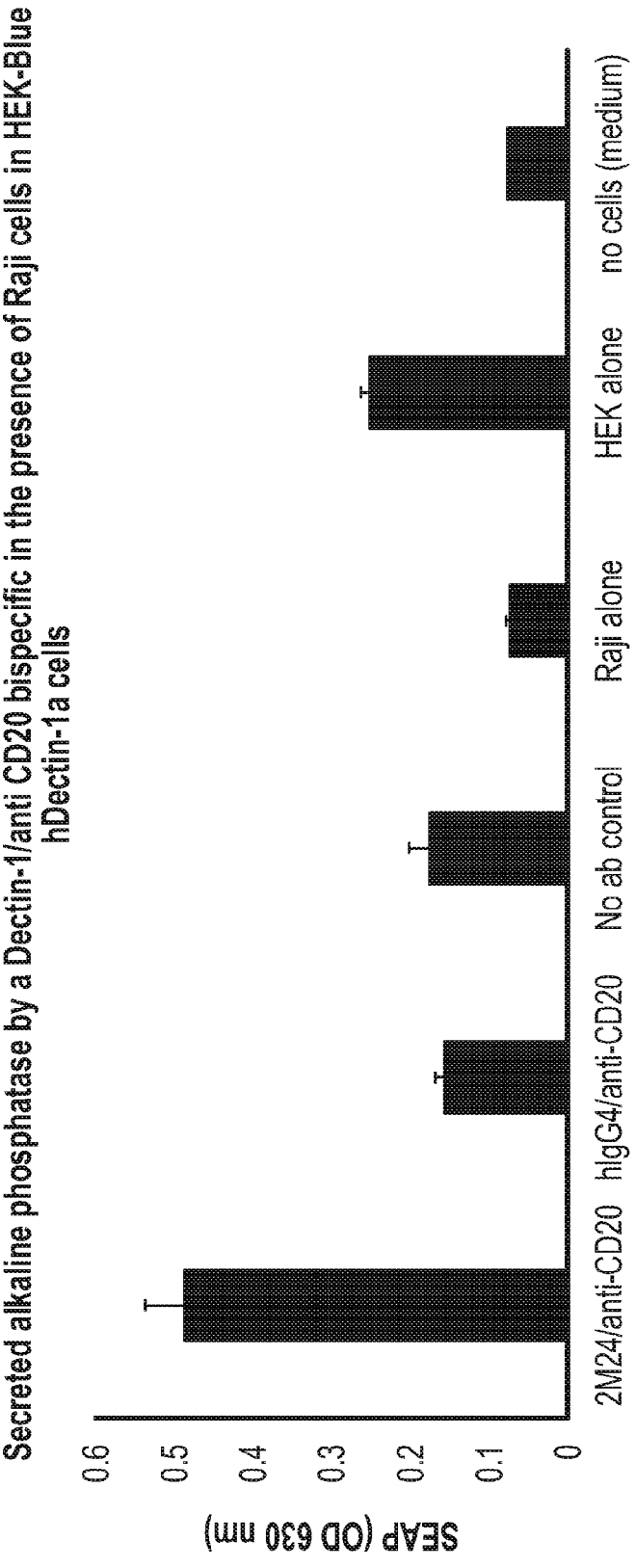

Secreted alkaline phosphatase by a Dectin-1/anti CD20 bispecific in the presence of Raji cells in HEK-Blue hDectin-1a cells
SEAP (OD 630 nm)
0.6
0.5
0.4
0.3
0.2
0.1
0
2M24/anti-CD20
hIgG4/anti-CD20
No ab control
Raji alone
HEK alone
no cells (medium)

FIG. 15

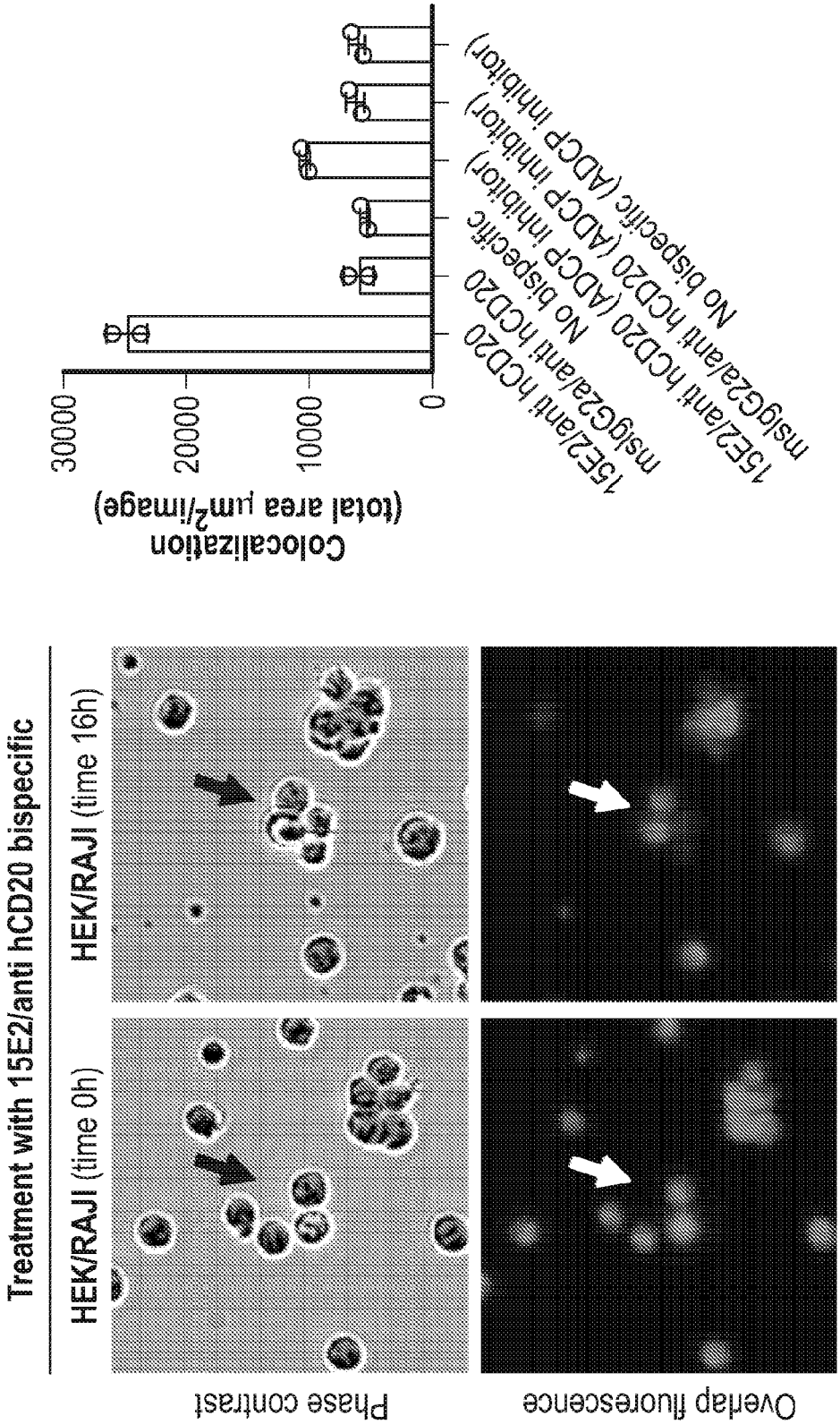

Treatment with 15E2/anti hCD20 bispecific
HEK/RAJI (time 0h)
HEK/RAJI (time 16h)
Phase contrast
Overlap fluorescence
Colocalization
(total area μm²/image)
30000
20000
10000
0
15E2/anti hCD20
msIgG2a/anti hCD20
No bispecific
15E2/anti hCD20 (ADCP inhibitor)
msIgG2a/anti hCD20 (ADCP inhibitor)
No bispecific (ADCP inhibitor)

FIG. 16

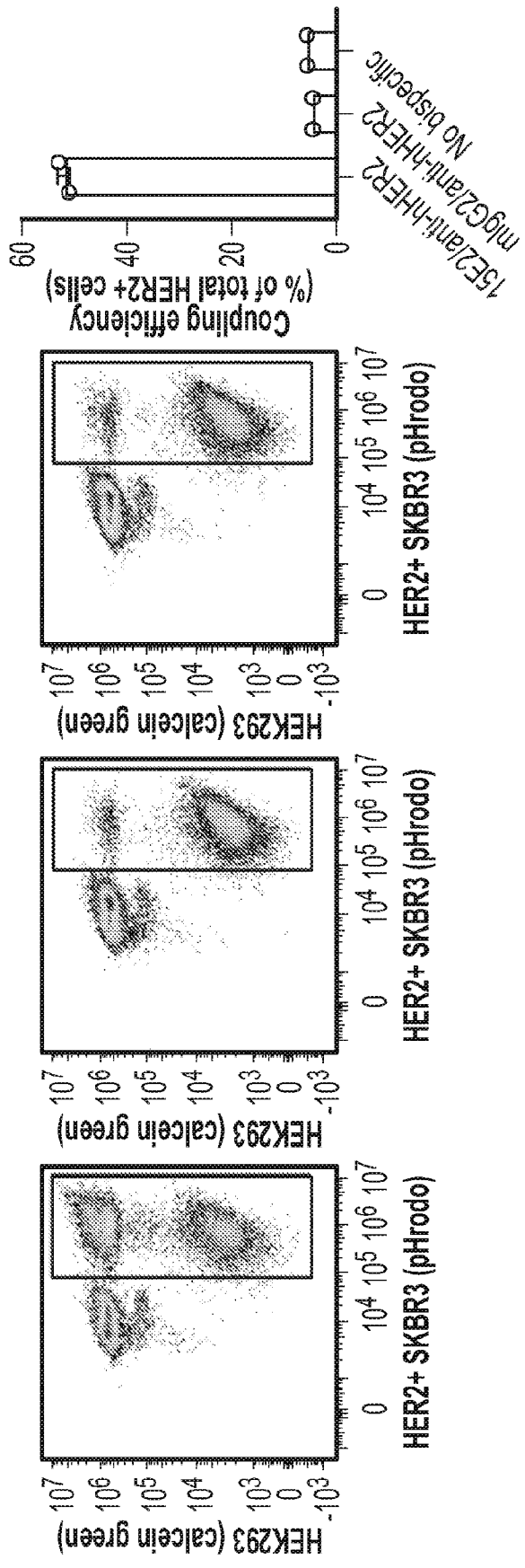

15E2/anti-hHER2
mIgG2/anti-hHER2
No bispecific
Coupling efficiency
(% of total HER2+ cells)
0
20
40
60
HEK293 (calcein green)
HER2+ SKBR3 (pHrodo)
-10^3
0
10^3
10^4
10^5
10^6
10^7

FIG. 17

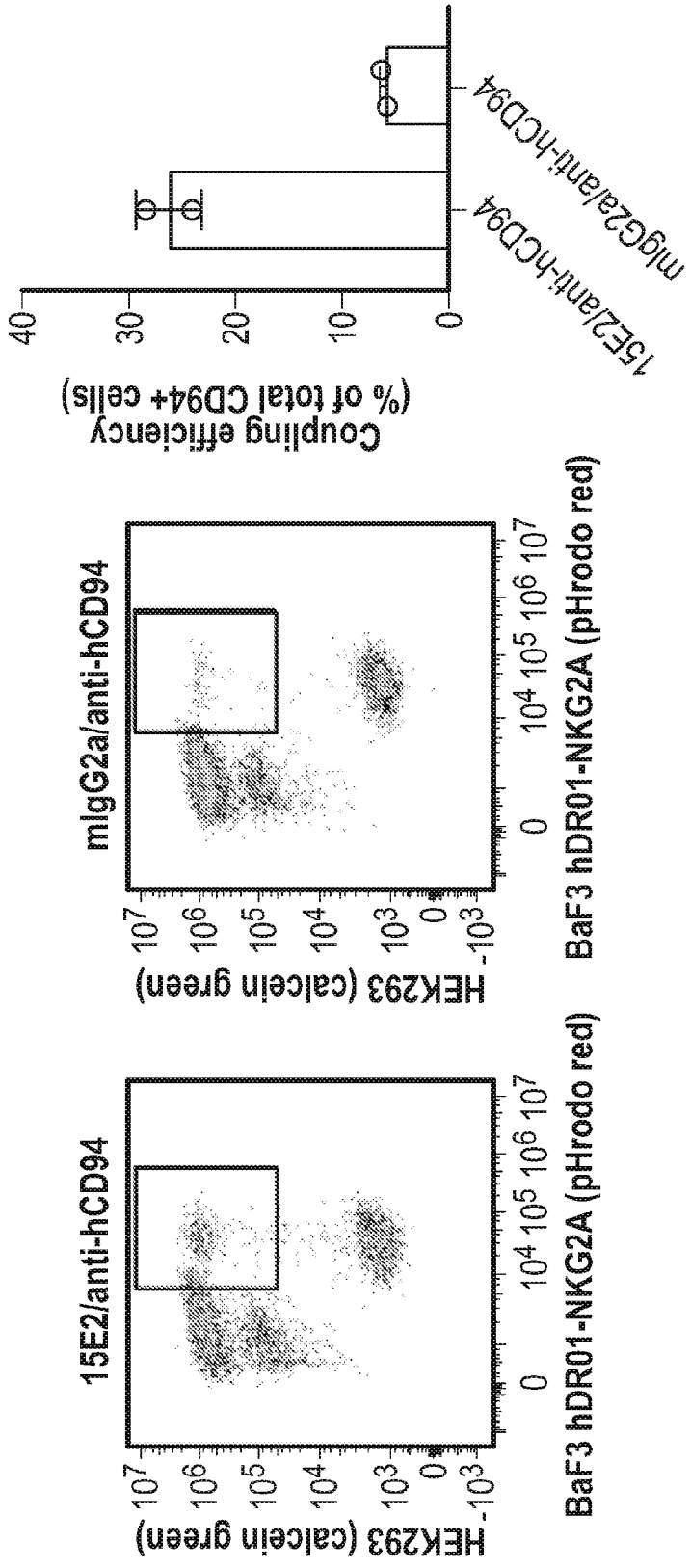

Coupling efficiency
(% of total CD94+ cells)
40
30
20
10
0
15E2/anti-hCD94
mIgG2a/anti-hCD94
mIgG2a/anti-hCD94
15E2/anti-hCD94
HEK293 (calcein green)
BaF3 hDR01-NKG2A (pHrodo red)
HEK293 (calcein green)
BaF3 hDR01-NKG2A (pHrodo red)

FIG. 18

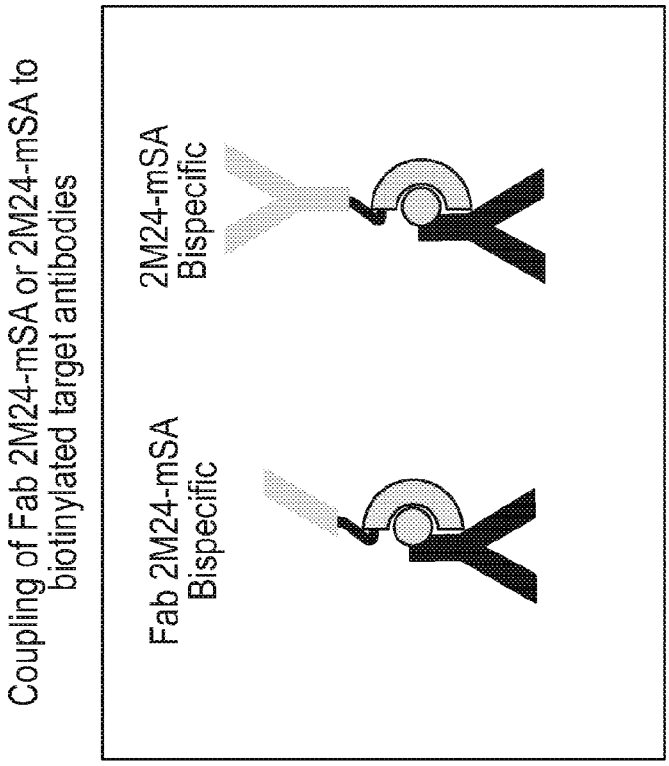


FIG. 19B

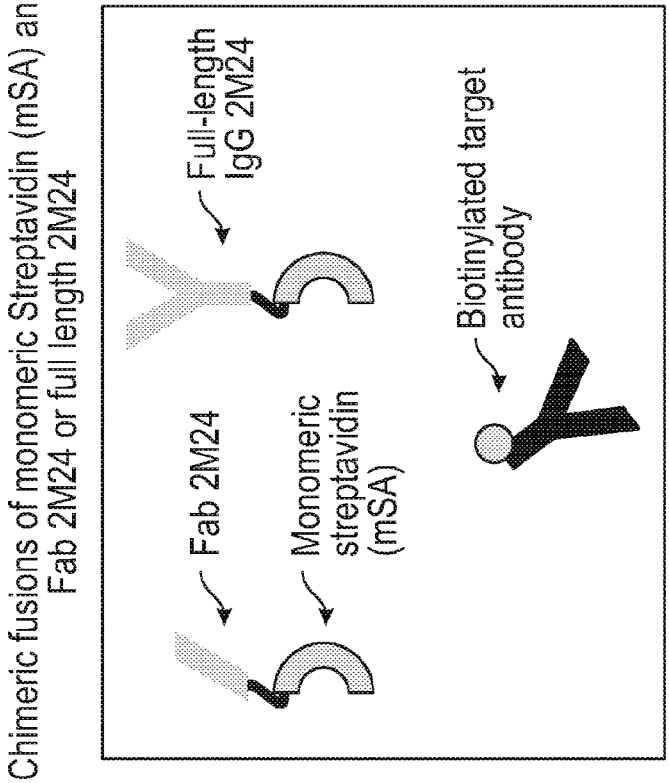


FIG. 19A

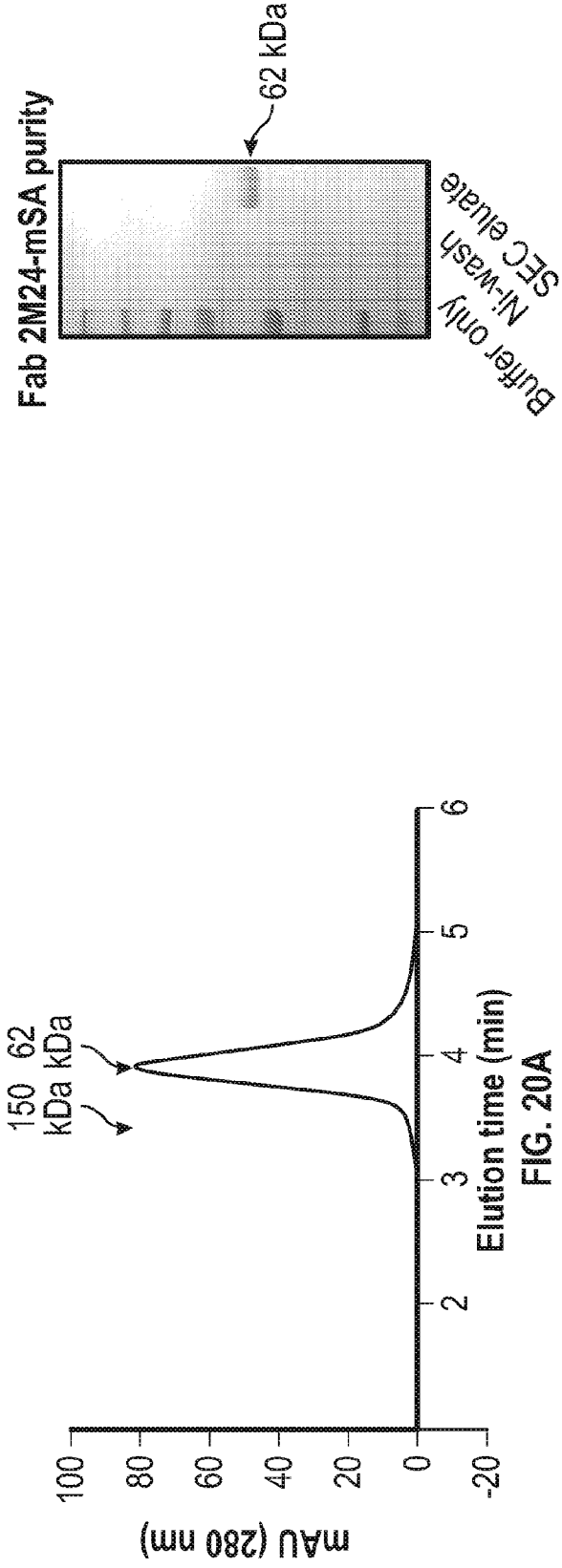


FIG. 20A

FIG. 20B

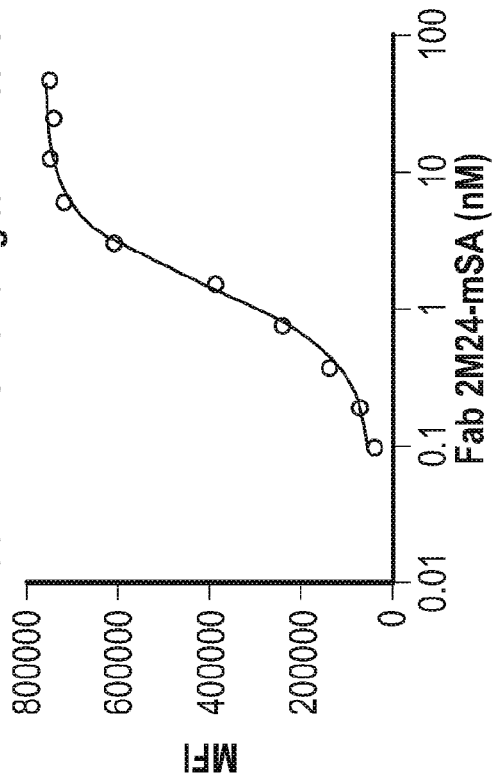


FIG. 20C

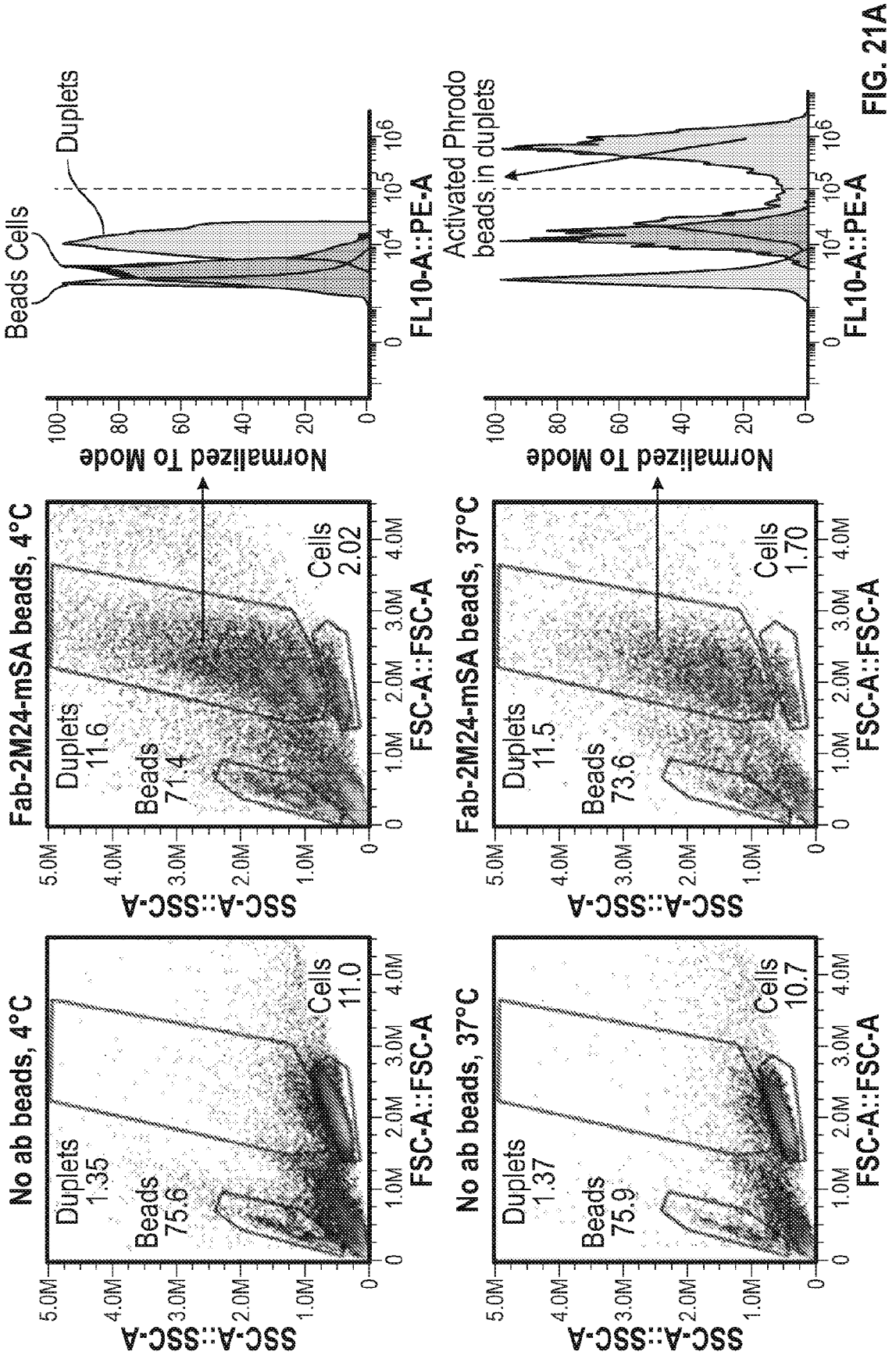

No ab beads, 4°C
Duplets 1.35
Beads 75.6
Cells 11.0
SSC-A::SSC-A
FSC-A::FSC-A
Fab-2M24-mSA beads, 4°C
Duplets 11.6
Beads 71.4
Cells 2.02
No ab beads, 37°C
Duplets 1.37
Beads 75.9
Cells 10.7
Fab-2M24-mSA beads, 37°C
Duplets 11.5
Beads 73.6
Cells 1.70
Normalized To Mode
Beads Cells
Duplets
FL10-A::PE-A
Activated Phrodo beads in duplets

FIG. 21A

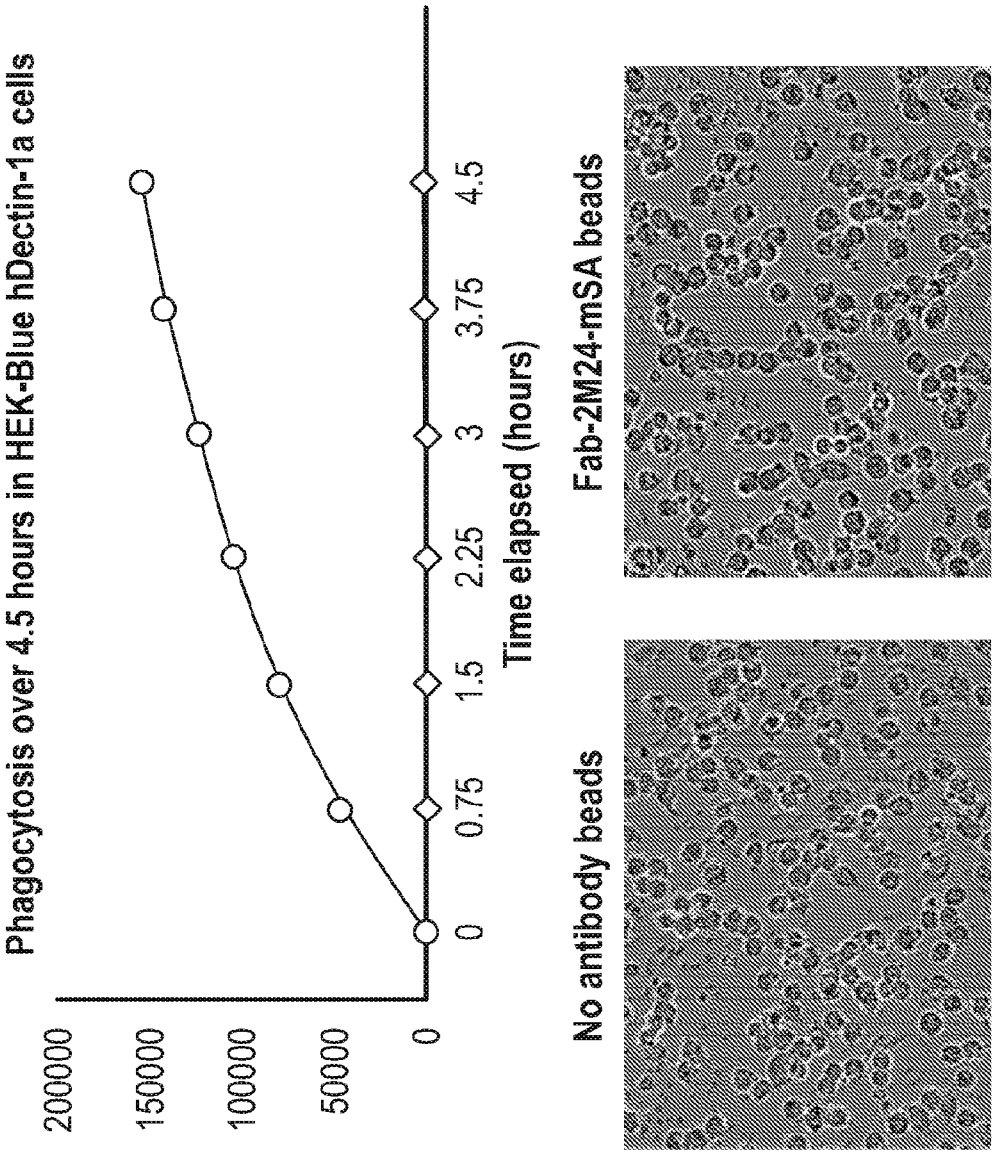

Phagocytosis over 4.5 hours in HEK-Blue hDectin-1a cells
red integrated intensity
200000
150000
100000
50000
0
0
0.75
1.5
2.25
3
3.75
4.5
Time elapsed (hours)
No antibody beads
Fab-2M24-mSA beads

FIG. 21B

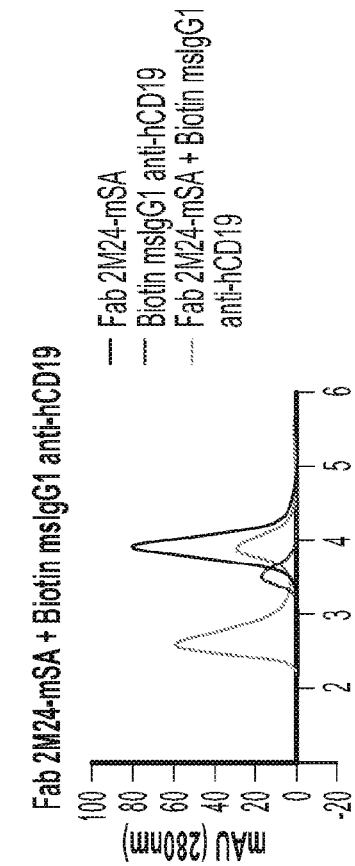


FIG. 22A

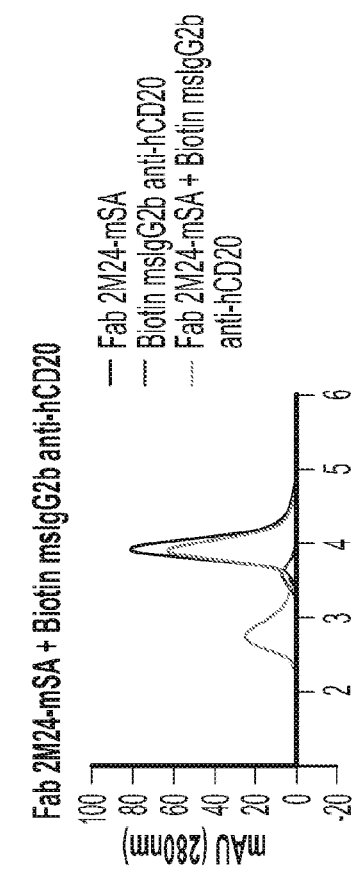


FIG. 22B

FIG. 22C

FIG. 22D

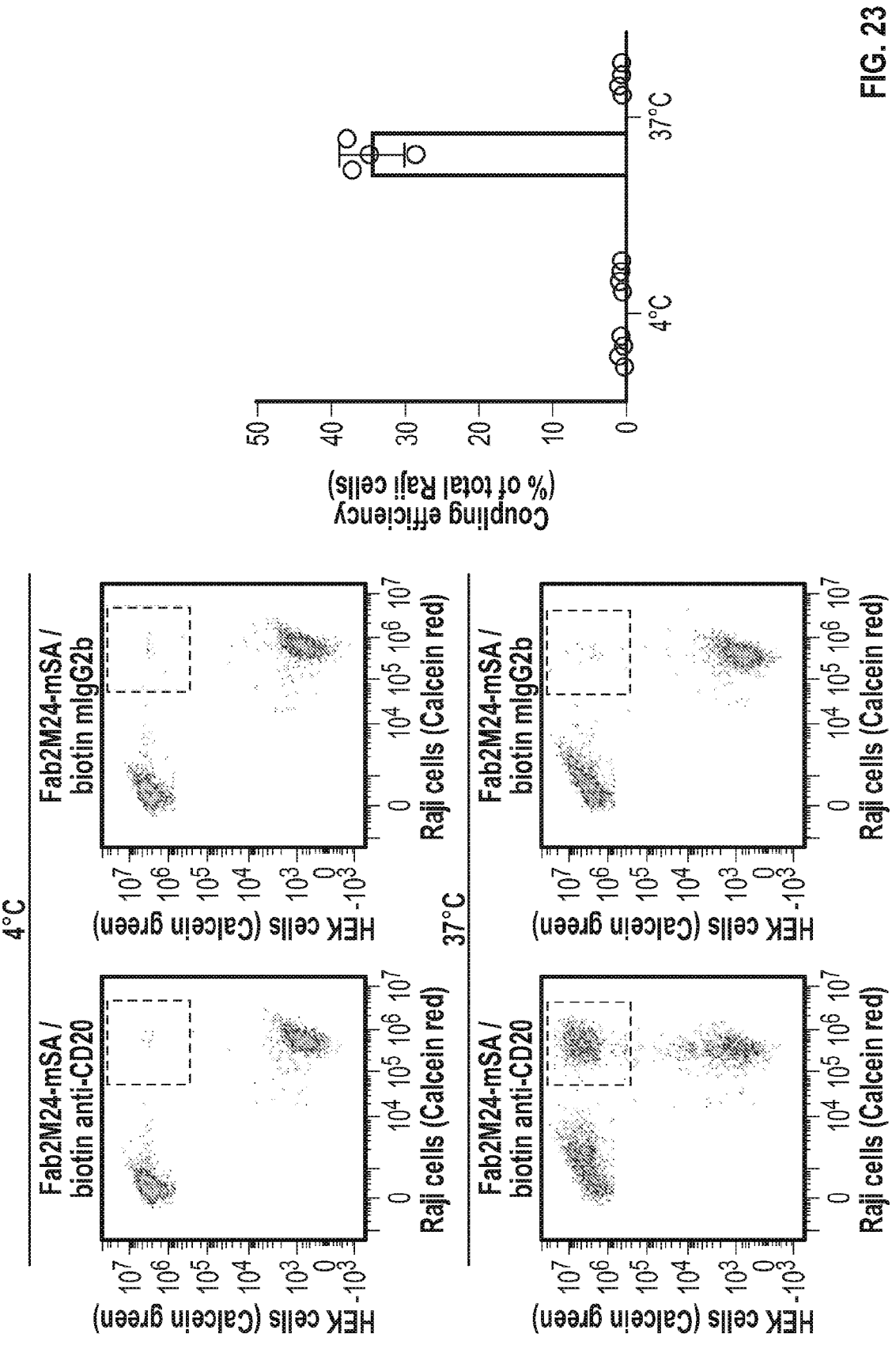

4°C
37°C
Fab2M24-mSA / biotin anti-CD20
Fab2M24-mSA / biotin mIgG2b
HEK cells (Calcein green)
Raji cells (Calcein red)
Coupling efficiency (% of total Raji cells)
4°C
37°C

FIG. 23

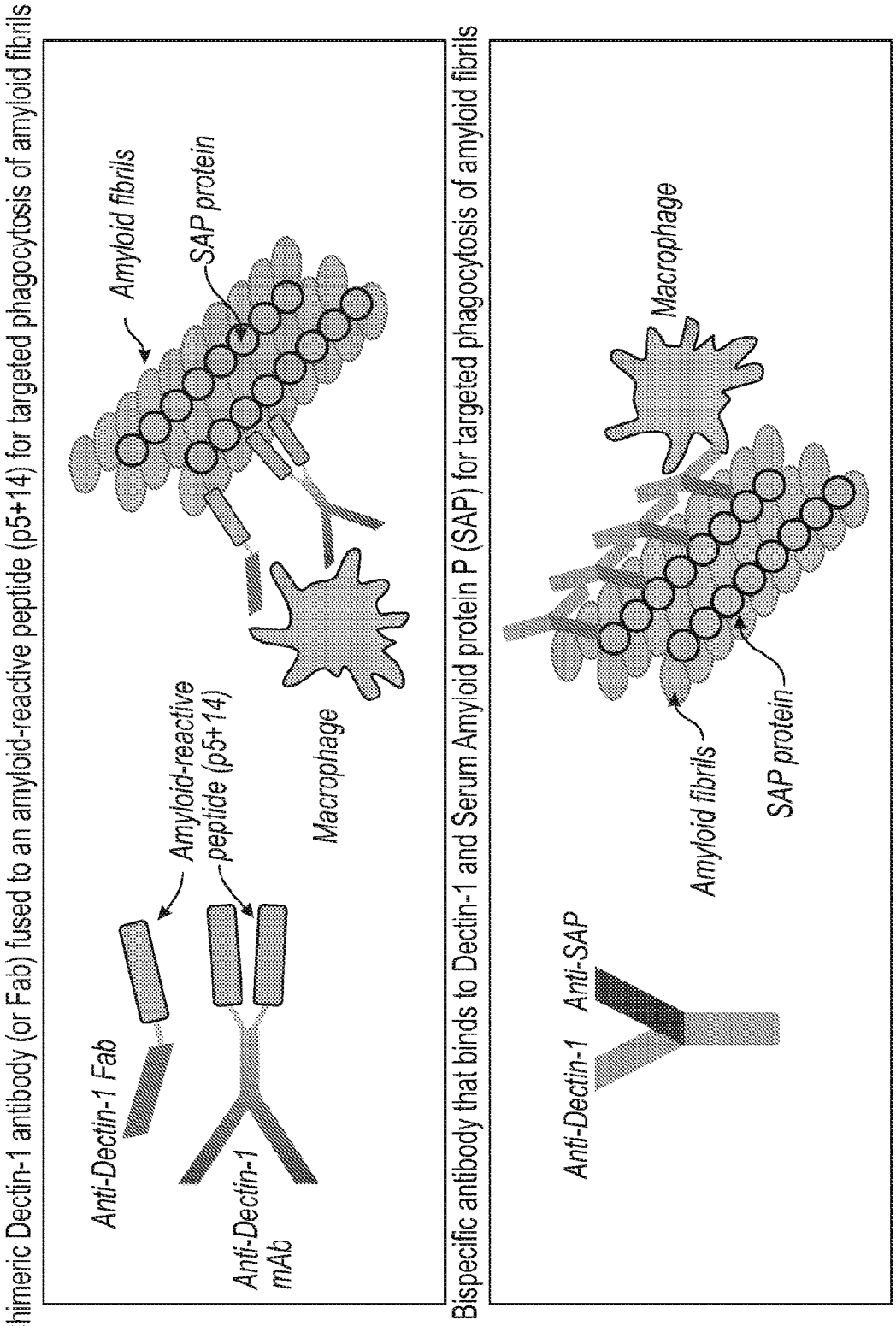

Chimeric Dectin-1 antibody (or Fab) fused to an amyloid-reactive peptide (p5+14) for targeted phagocytosis of amyloid fibrils
Anti-Dectin-1 Fab
Amyloid-reactive peptide (p5+14)
Anti-Dectin-1 mAb
Amyloid fibrils
SAP protein
Macrophage
Bispecific antibody that binds to Dectin-1 and Serum Amyloid protein P (SAP) for targeted phagocytosis of amyloid fibrils
Anti-Dectin-1
Anti-SAP
Amyloid fibrils
SAP protein
Macrophage

FIG. 24

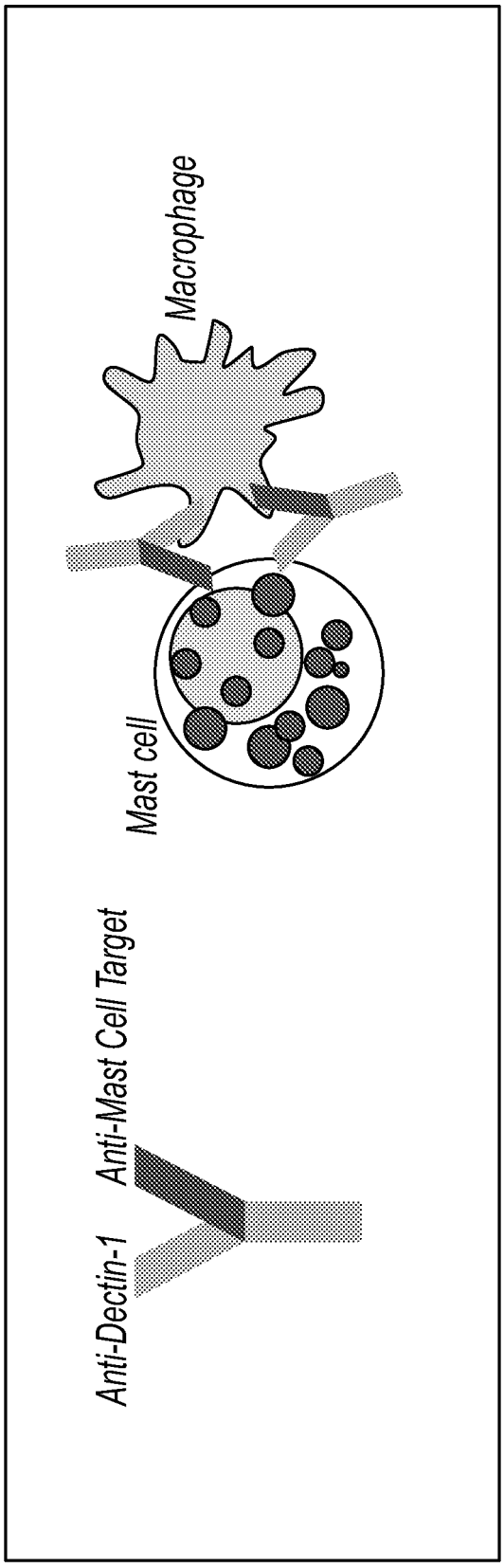


FIG. 25A

Targets identified by proteomics studies	*Targets identified by RNA sequencing of mastocytosis patients samples*
MRGPRX2	CD33 (SIGLEC 3)
CD171 (L1CAM)	CD25 (IL25Ra)
SIGLEC 6	CD30 (TNFRFS8)
CD117	SIGLEC 8
CD203c	CD13
CD51	CD44
DPP4	CD52
	CD117
	CD123

FIG. 25B

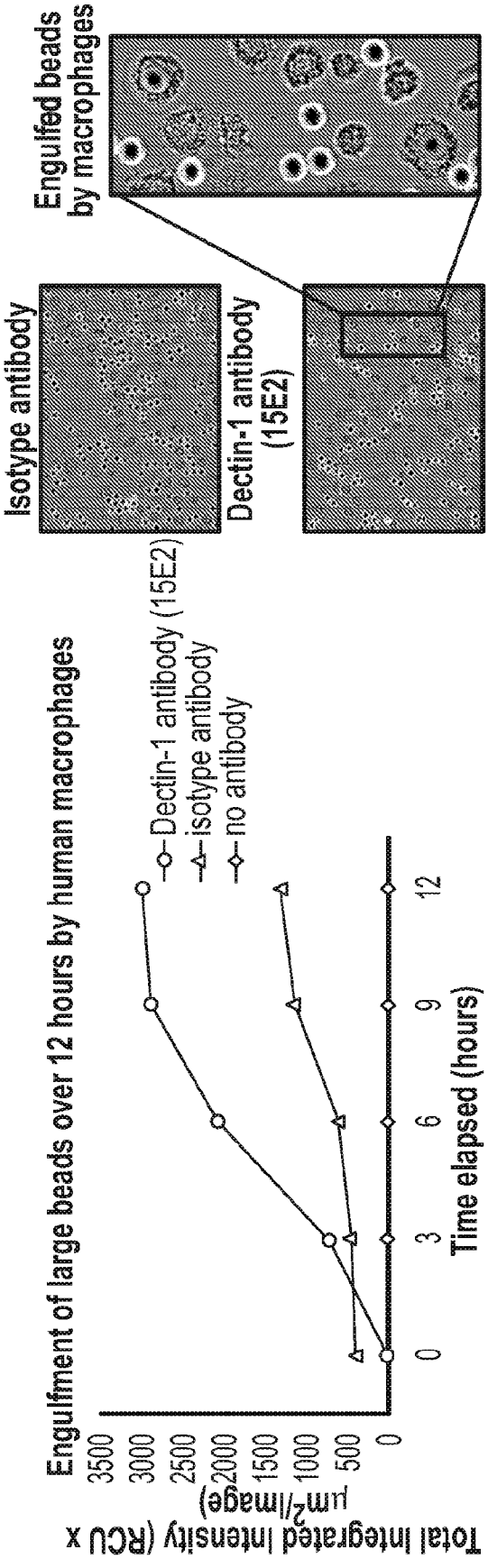

Engulfed beads by macrophages
Isotype antibody
Dectin-1 antibody (15E2)
Engulfment of large beads over 12 hours by human macrophages
Total Integrated Intensity (RCU x μm²/Image)
3500
3000
2500
2000
1500
1000
500
0
0
3
6
9
12
Time elapsed (hours)
Dectin-1 antibody (15E2)
isotype antibody
no antibody

FIG. 26

Bispecific(anti-Dectin-1/anti-microbialtarget) against bacteria, viruses, and fungi
Anti-Dectin-1
Anti-Bacterial Target
Anti-Dectin-1
Anti-Viral Target
Anti-Dectin-1
Anti-Fungal Target
Dectin-1 bispecific antibodies deploys Dectin-1-expressing phagocytes to eliminate bacterial, viral or fungal pathogens
Fungal particle
Monocyte
Bacterium
Virus
Fungal particle
Macrophage
Bacterium
Virus

FIG. 27

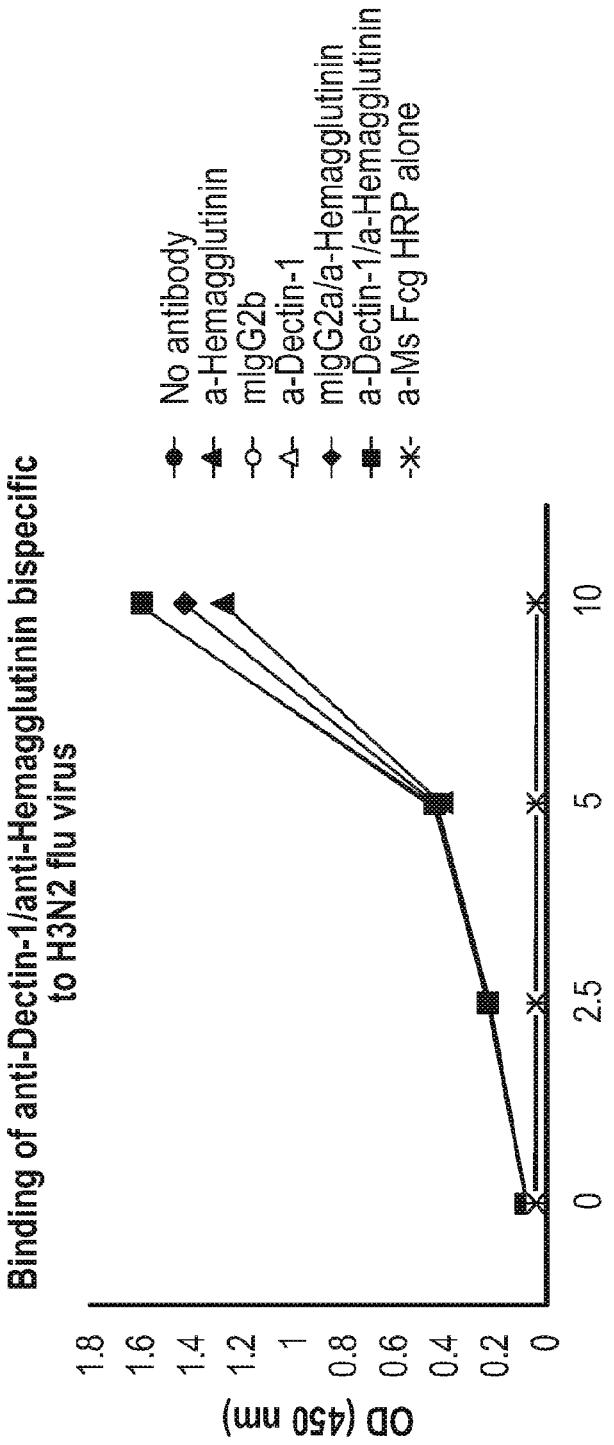

Binding of anti-Dectin-1/anti-Hemagglutinin bispecific to H3N2 flu virus
OD (450 nm)
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
0
2.5
5
10
H32N2 (ug/ml)
No antibody
a-Hemagglutinin
mIgG2b
a-Dectin-1
mIgG2a/a-Hemagglutinin
a-Dectin-1/a-Hemagglutinin
a-Ms Fcg HRP alone

FIG. 28A

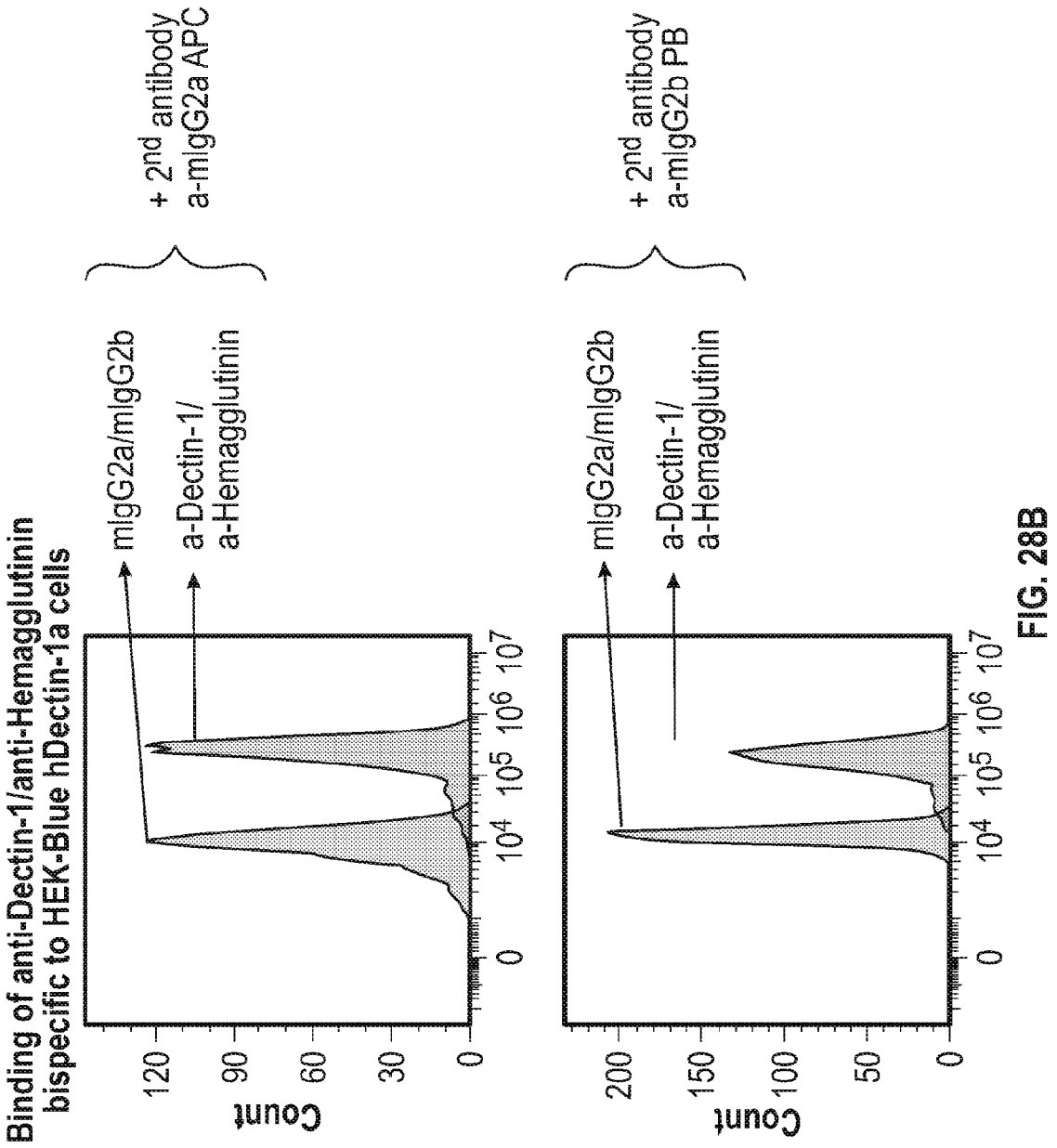

Binding of anti-Dectin-1/anti-Hemagglutinin bispecific to HEK-Blue hDectin-1a cells
mIgG2a/mIgG2b
a-Dectin-1/ a-Hemagglutinin
+ 2nd antibody a-mIgG2a APC
+ 2nd antibody a-mIgG2b PB
Count
0
30
60
90
120
50
100
150
200
0
10^4
10^5
10^6
10^7

FIG. 28B

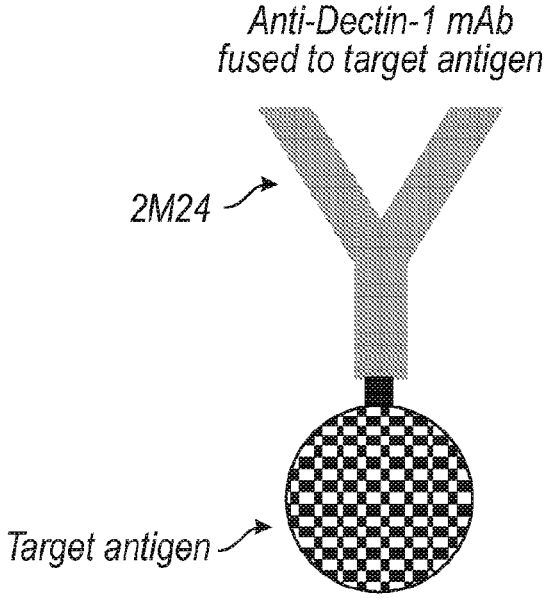

Anti-Dectin-1 mAb
fused to target antigen
2M24
Target antigen

FIG. 29A

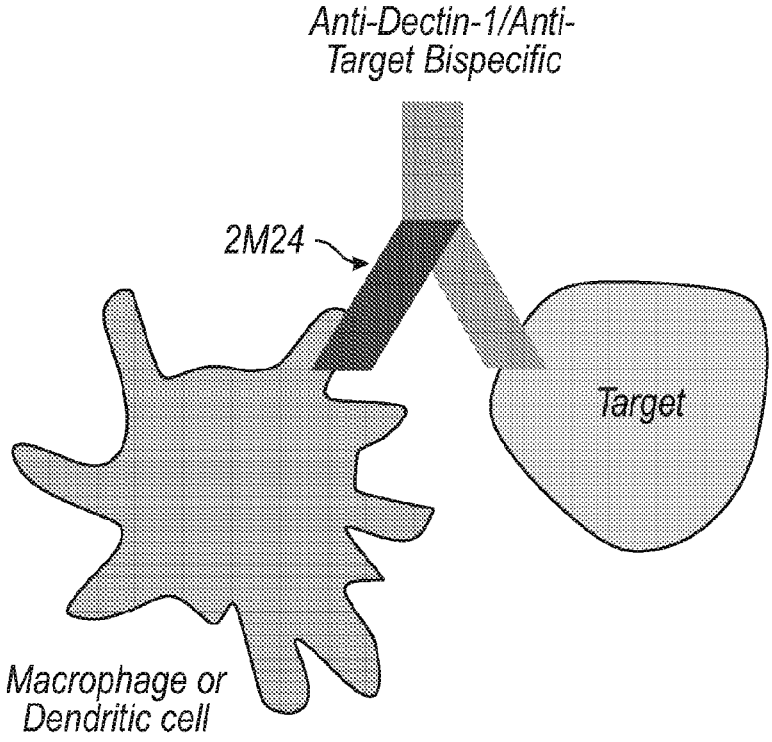

Anti-Dectin-1/Anti-
Target Bispecific
2M24
Target
Macrophage or
Dendritic cell

FIG. 29B

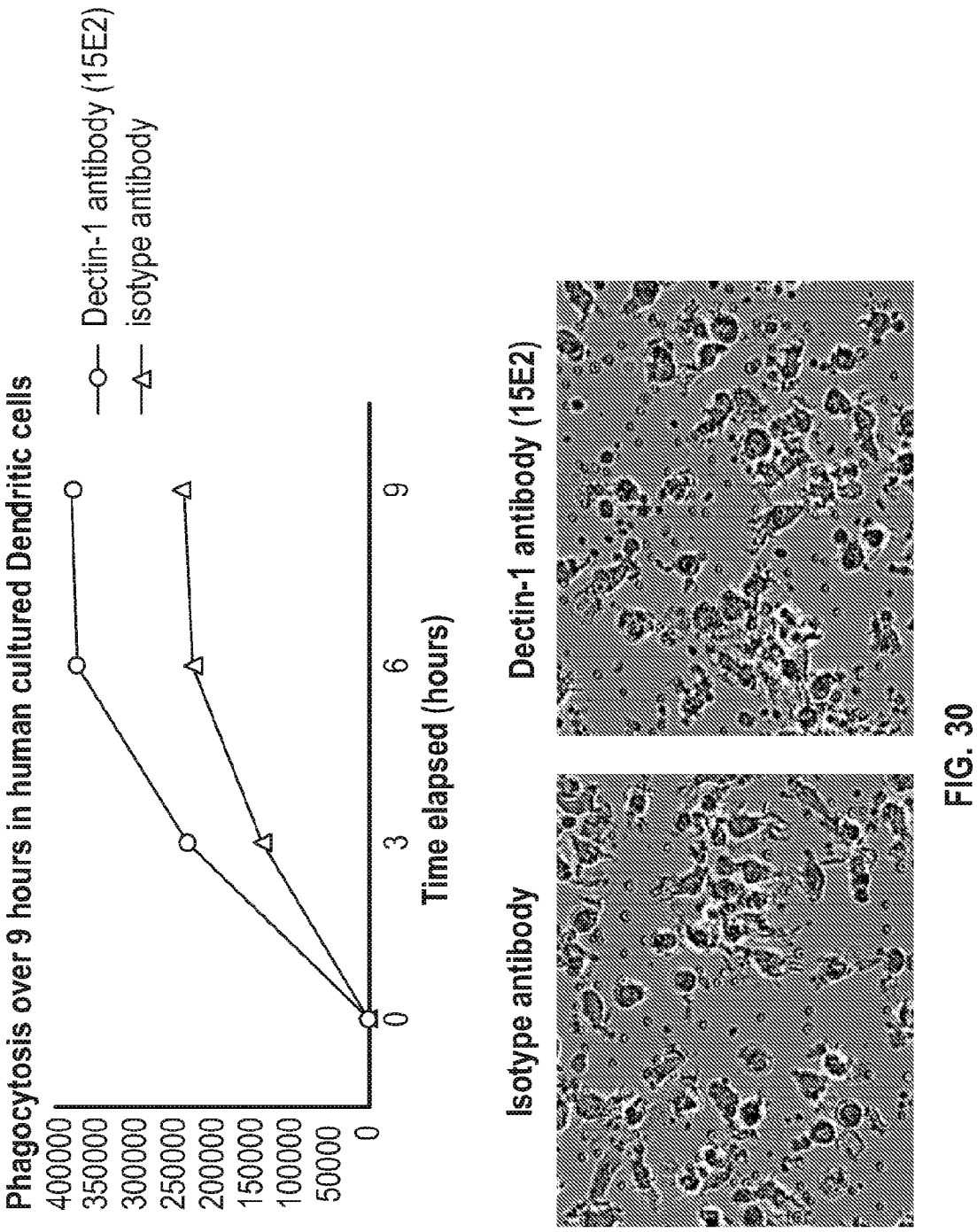

Phagocytosis over 9 hours in human cultured Dendritic cells
Total Integrated Intensity (RCU x μm²/image)
400000
350000
300000
250000
200000
150000
100000
50000
0
0
3
6
9
Time elapsed (hours)
Dectin-1 antibody (15E2)
isotype antibody
Isotype antibody
Dectin-1 antibody (15E2)

FIG. 30

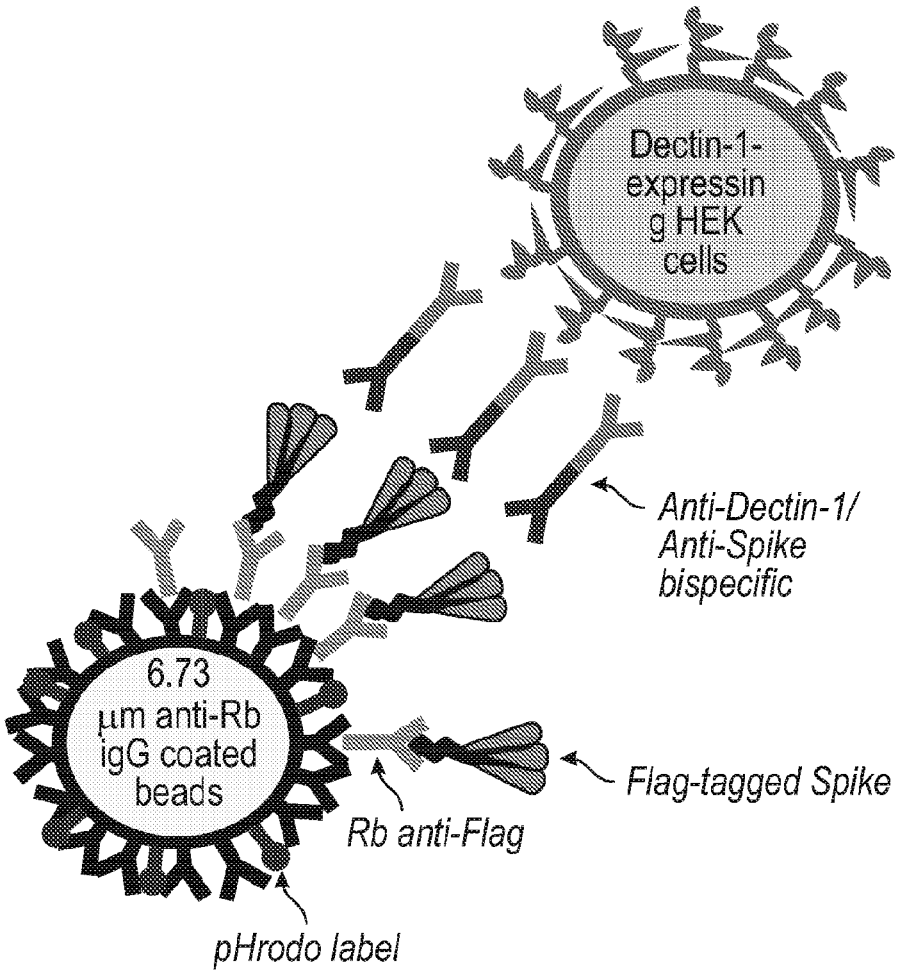

Dectin-1-expressing HEK cells
Anti-Dectin-1/ Anti-Spike bispecific
6.73 µm anti-Rb IgG coated beads
Flag-tagged Spike
Rb anti-Flag
pHrodo label

FIG. 31A

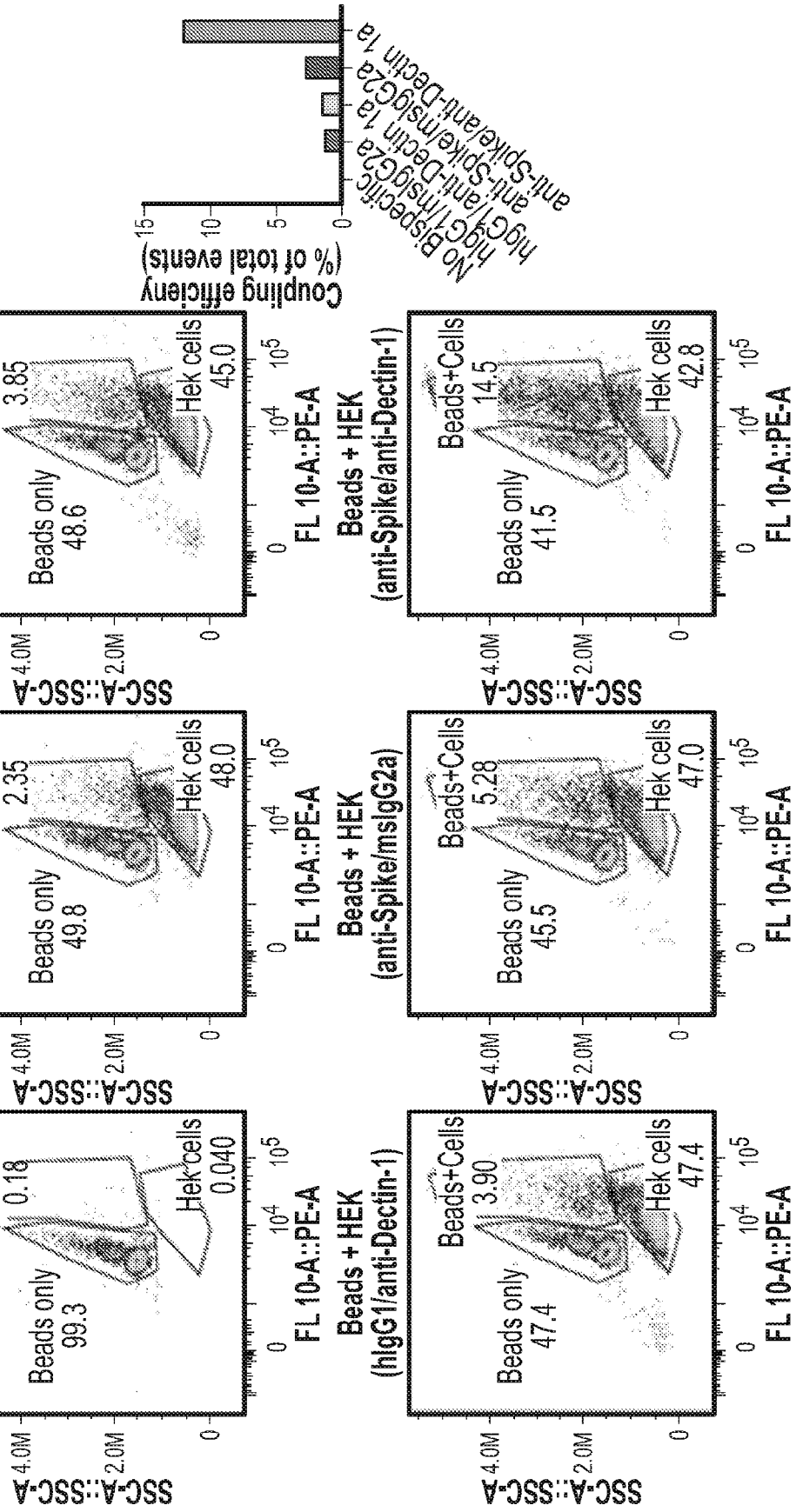

Beads only
Beads+Cells
0.18
Beads only
99.3
Hek cells
0.040
SSC-A::SSC-A
FL 10-A::PE-A
Beads + HEK
(No bispecific)
Beads+Cells
2.35
Beads only
49.8
Hek cells
48.0
Beads + HEK
(hIgG1/anti-Dectin-1)
Beads+Cells
3.90
Beads only
47.4
Hek cells
47.4
Beads + HEK
(anti-Spike/mIgG2a)
Beads+Cells
5.28
Beads only
45.5
Hek cells
47.0
Beads + HEK
(hIgG1/mIgG2a)
Beads+Cells
3.85
Beads only
48.6
Hek cells
45.0
Beads + HEK
(anti-Spike/anti-Dectin-1)
Beads+Cells
14.5
Beads only
41.5
Hek cells
42.8
Coupling efficiency
(% of total events)
No Bispecific
hIgG1/mIgG2a
anti-Spike/mIgG2a
anti-Spike/anti-Dectin 1a

FIG. 31B

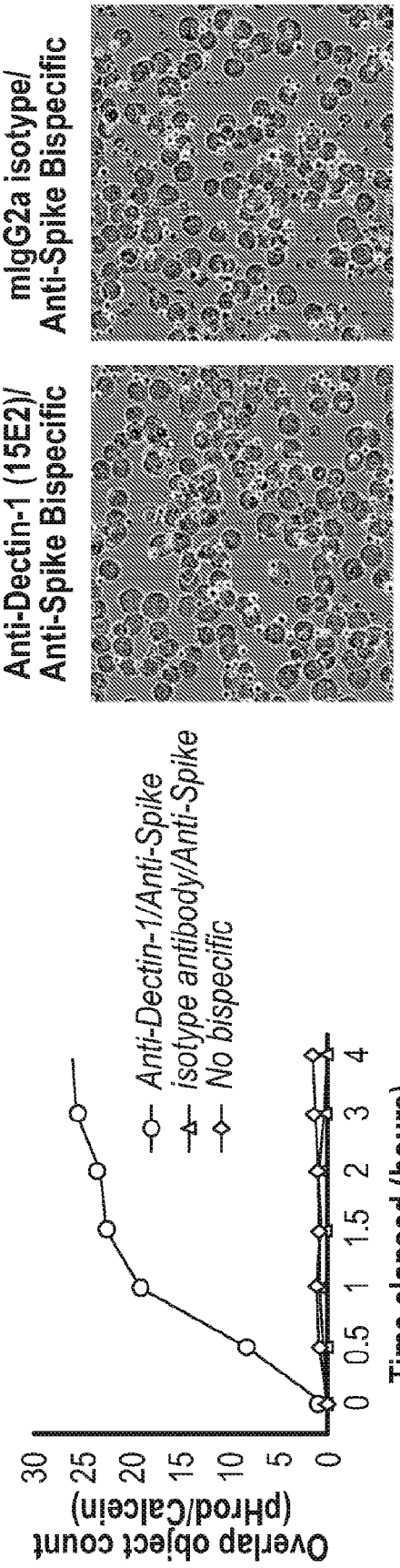

Anti-Dectin-1 (15E2)/
Anti-Spike Bispecific
mIgG2a isotype/
Anti-Spike Bispecific
Overlap object count
(pHrod/Calcein)
30
25
20
15
10
5
0
0
0.5
1
1.5
2
3
4
Time elapsed (hours)
Anti-Dectin-1/Anti-Spike
isotype antibody/Anti-Spike
No bispecific

FIG. 31C

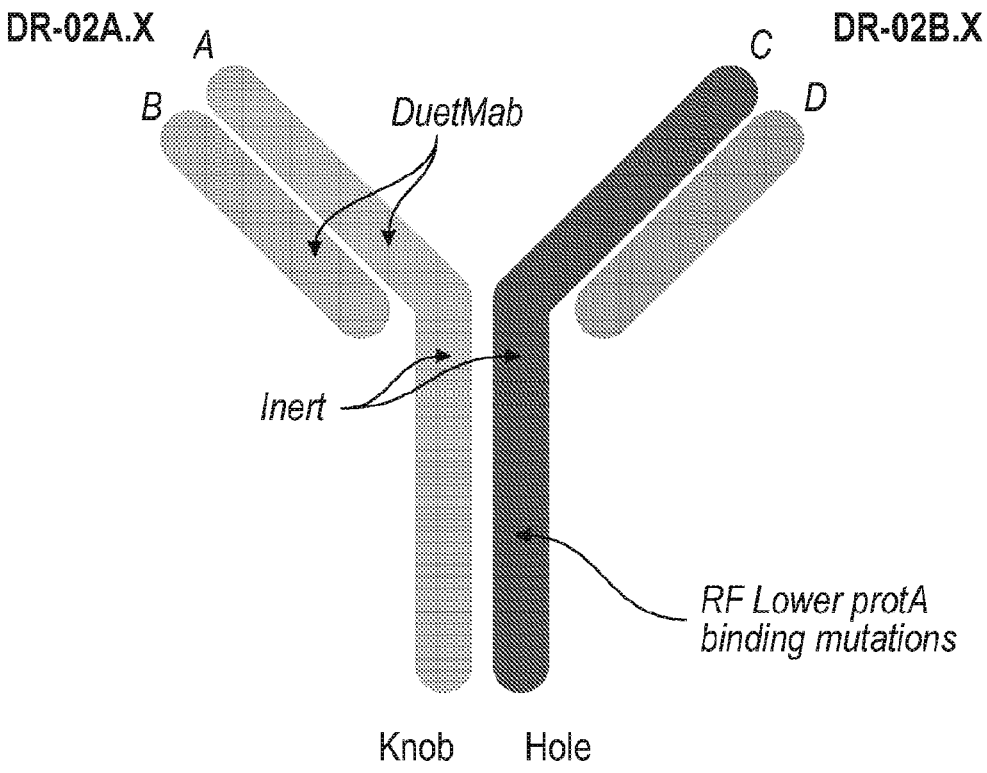

DR-02A.X
A
B
DuetMab
C
D
DR-02B.X
Inert
RF Lower protA
binding mutations
Knob
Hole

FIG. 32A

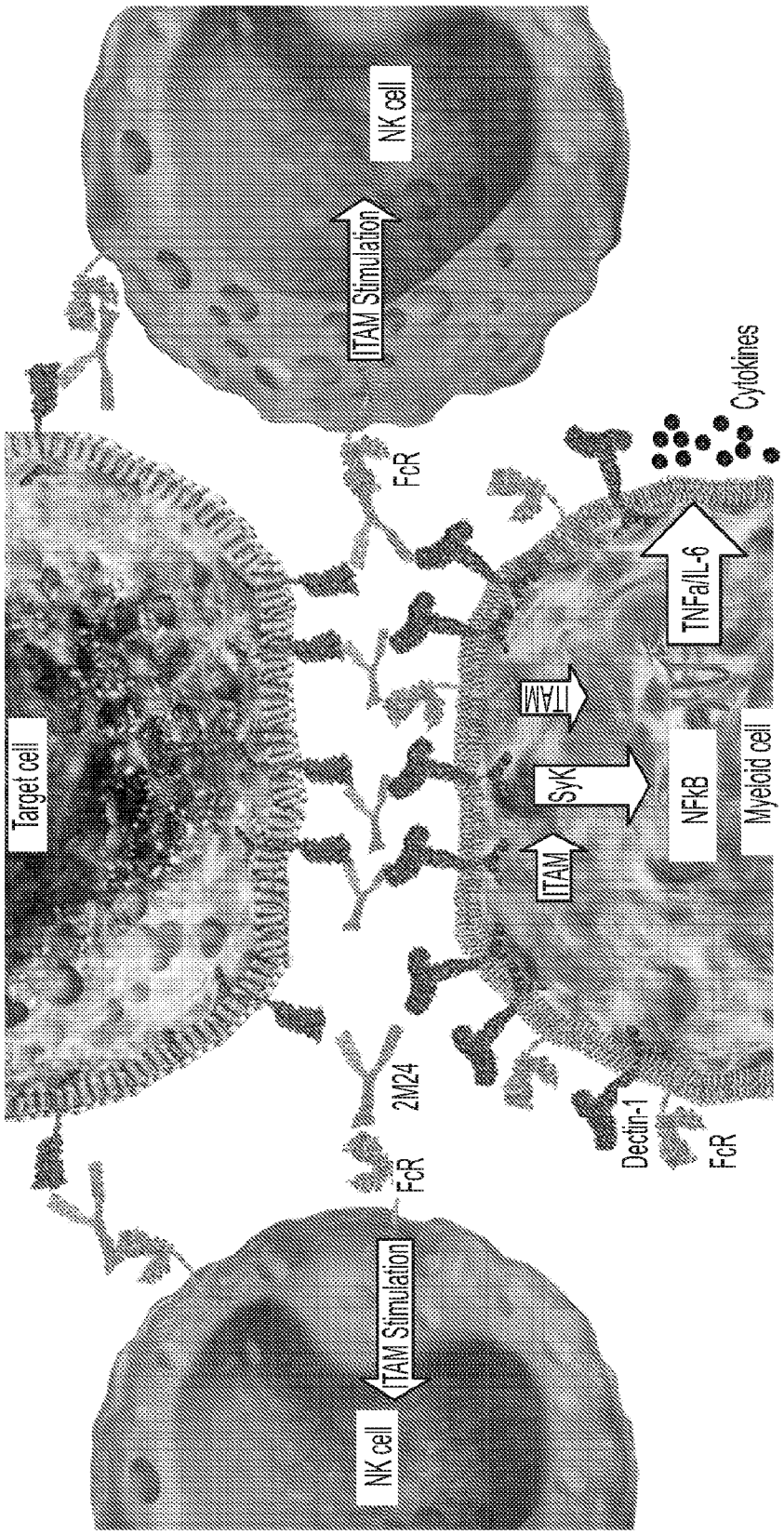

NK cell
ITAM Stimulation
FcR
Cytokines
TNFa/IL-6
Target cell
ITAM
SyK
ITAM
NFkB
Myeloid cell
2M24
Dectin-1
FcR
FcR
ITAM Stimulation
NK cell

FIG. 32B

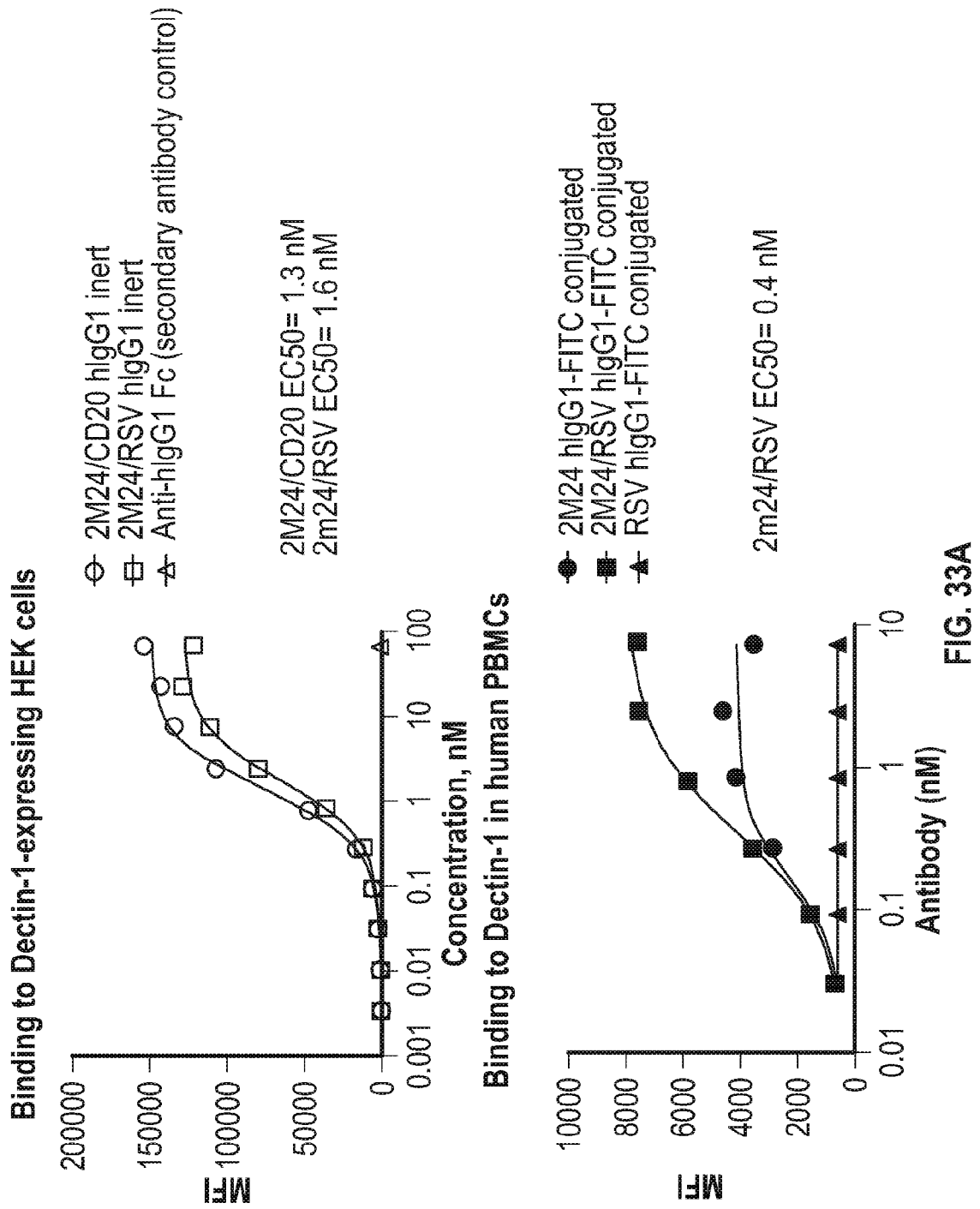

Binding to Dectin-1-expressing HEK cells
2M24/CD20 hIgG1 inert
2M24/RSV hIgG1 inert
Anti-hIgG1 Fc (secondary antibody control)
2M24/CD20 EC50= 1.3 nM
2m24/RSV EC50= 1.6 nM
MFI
Concentration, nM
Binding to Dectin-1 in human PBMCs
2M24 hIgG1-FITC conjugated
2M24/RSV hIgG1-FITC conjugated
RSV hIgG1-FITC conjugated
2m24/RSV EC50= 0.4 nM
MFI
Antibody (nM)

FIG. 33A

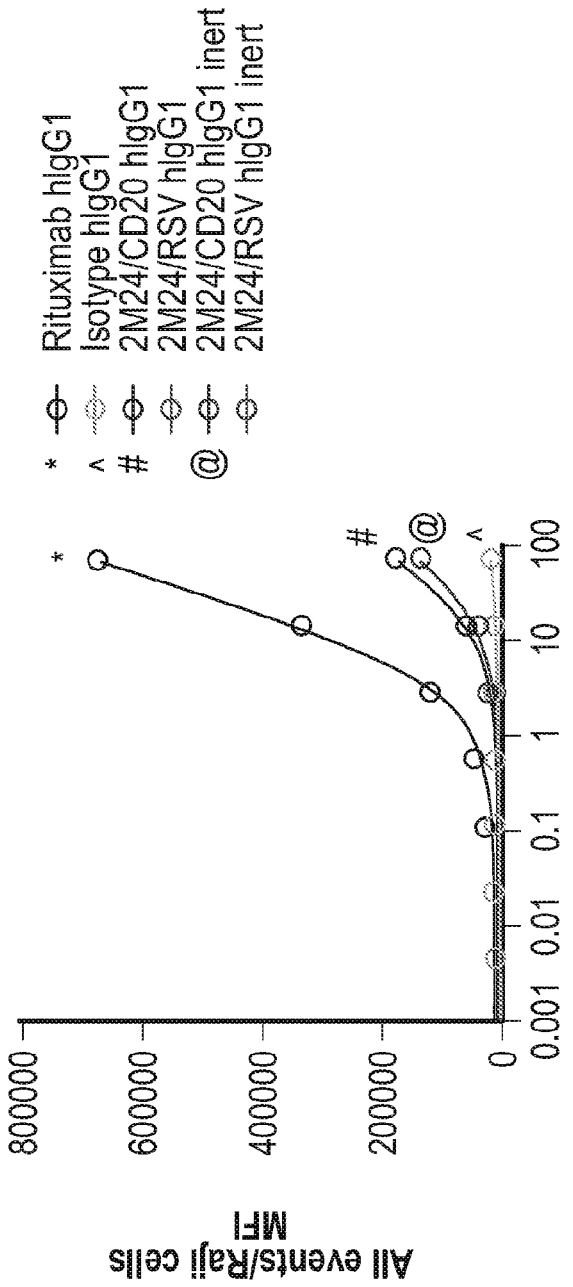

Rituximab hIgG1
Isotype hIgG1
2M24/CD20 hIgG1
2M24/RSV hIgG1
2M24/CD20 hIgG1 inert
2M24/RSV hIgG1 inert
All events/Raji cells MFI
800000
600000
400000
200000
0
0.001
0.01
0.1
1
10
100
Concentration, nM

FIG. 33B

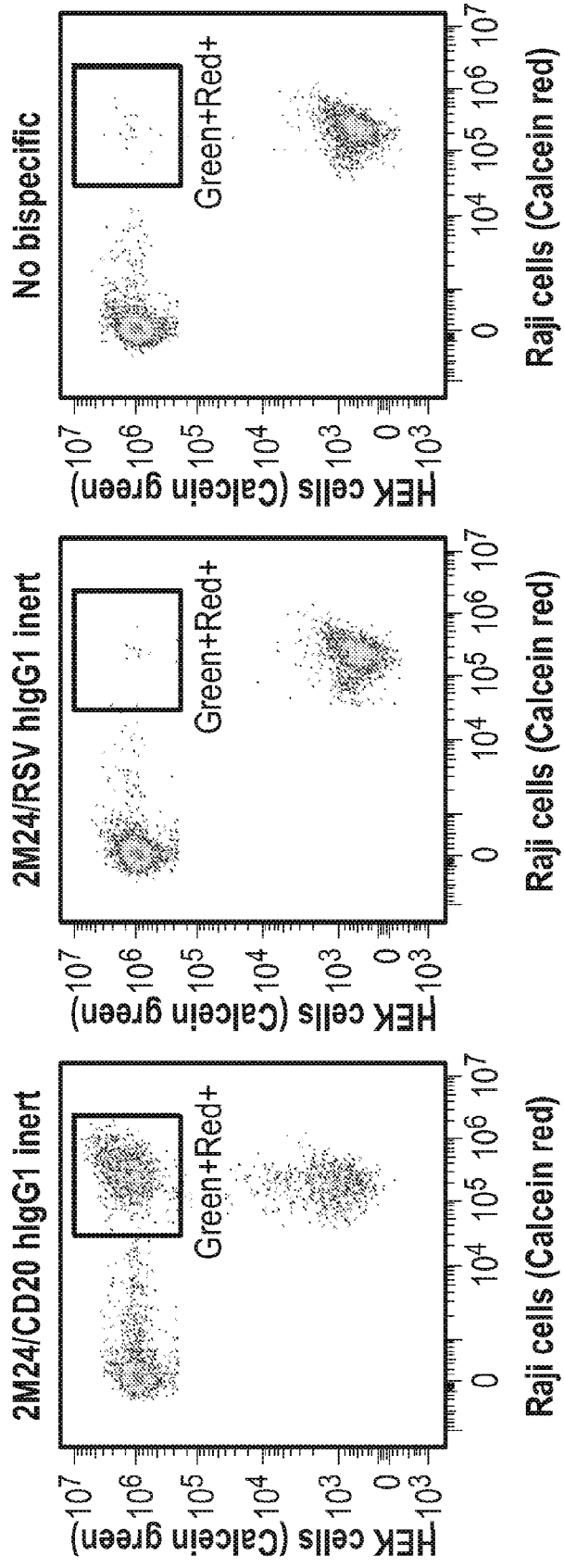

2M24/CD20 hIgG1 inert
2M24/RSV hIgG1 inert
No bispecific
Green+Red+
HEK cells (Calcein green)
Raji cells (Calcein red)
10^7
10^6
10^5
10^4
10^3
0

FIG. 34A

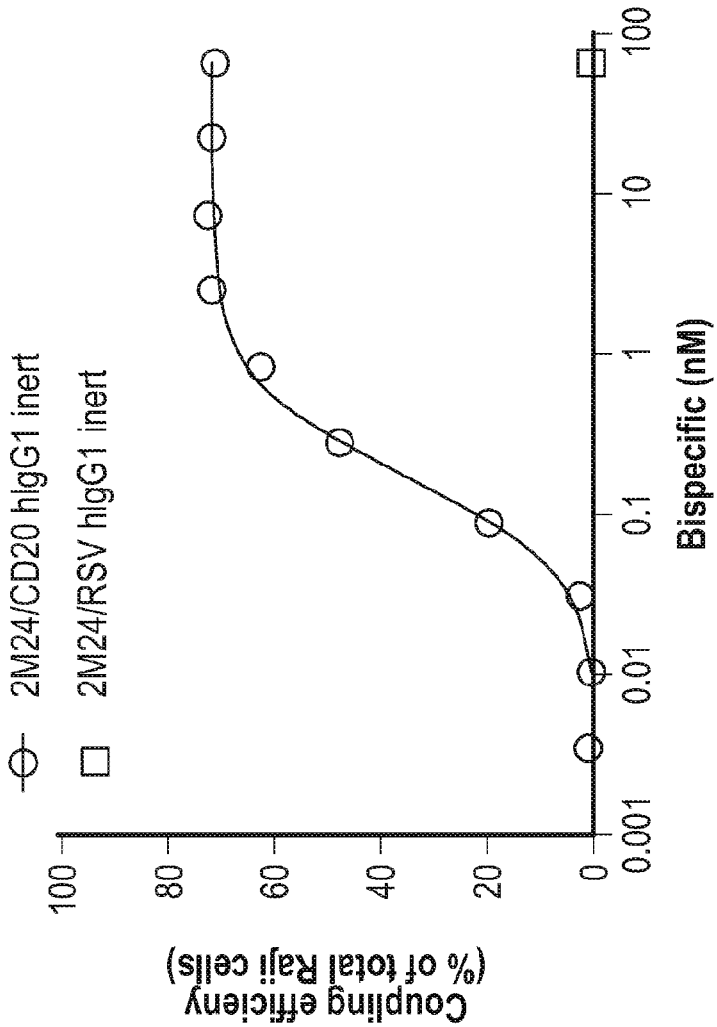

2M24/CD20 hIgG1 inert
2M24/RSV hIgG1 inert
Coupling efficiency
(% of total Raji cells)
100
80
60
40
20
0
0.001
0.01
0.1
1
10
100
Bispecific (nM)

FIG. 34B

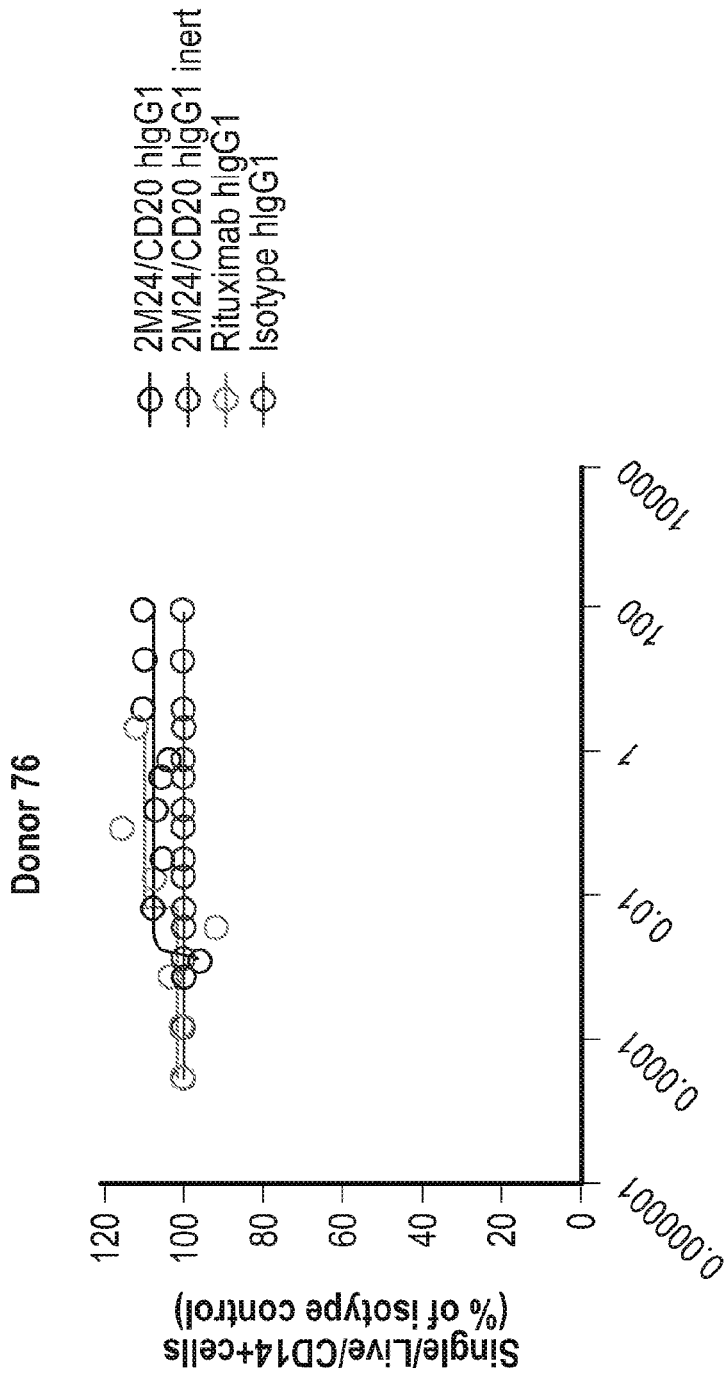

Donor 76
2M24/CD20 hIgG1
2M24/CD20 hIgG1 inert
Rituximab hIgG1
Isotype hIgG1
Single/Live/CD14+cells
(% of isotype control)
120
100
80
60
40
20
0
0.00001
0.0001
0.01
1
100
10000
Concentration (nM)

FIG. 35A

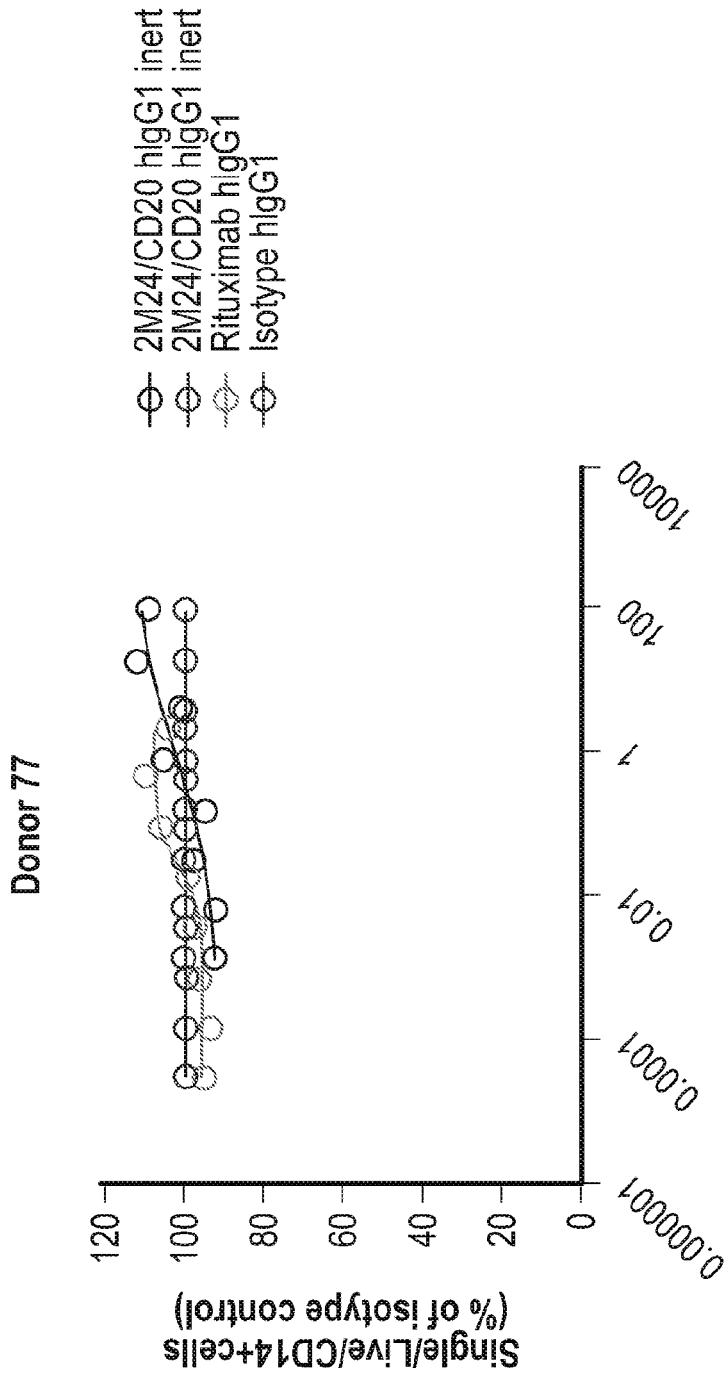

Donor 77
Single/Live/CD14+cells
(% of isotype control)
120
100
80
60
40
20
0
0.00001
0.0001
0.01
1
100
10000
Concentration (nM)
2M24/CD20 hIgG1 inert
2M24/CD20 hIgG1 inert
Rituximab hIgG1
Isotype hIgG1

FIG. 35B

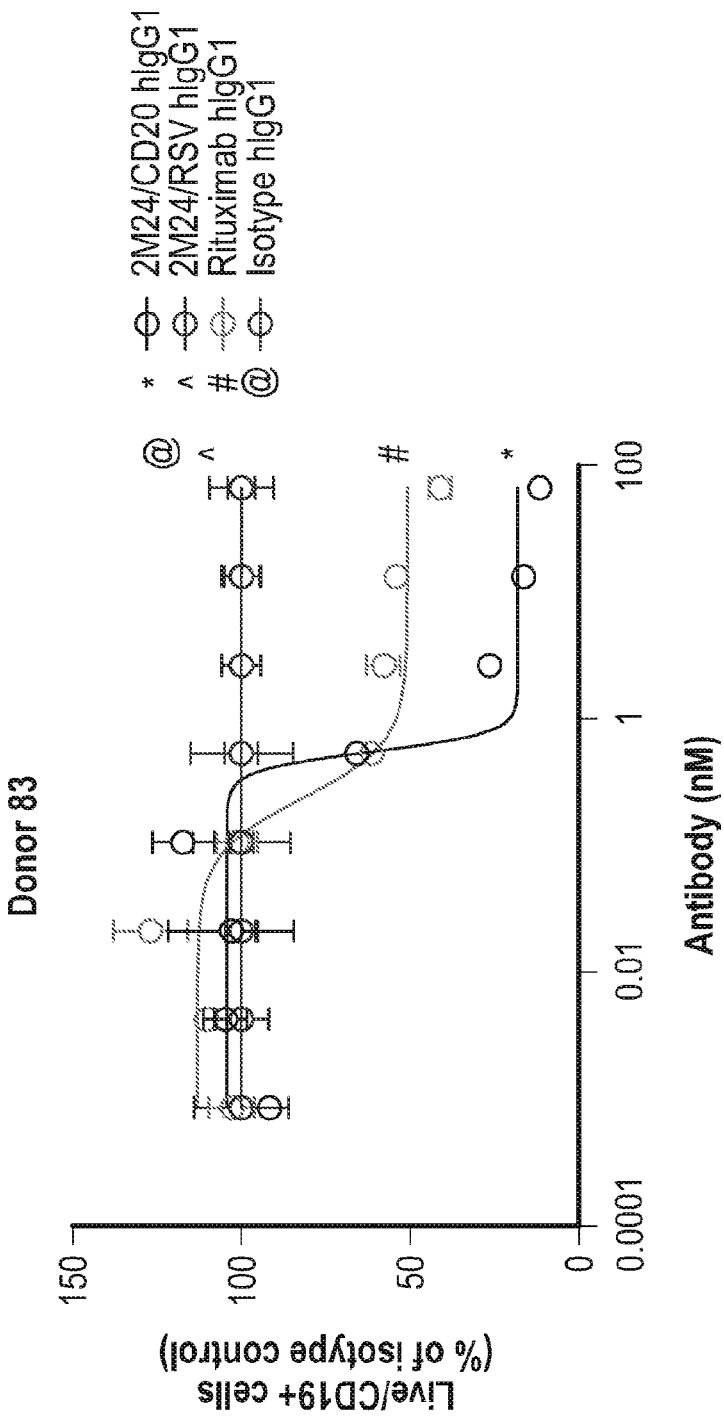

Donor 83
Live/CD19+ cells
(% of isotype control)
150
100
50
0
0.0001
0.01
1
100
Antibody (nM)
* 2M24/CD20 hIgG1
^ 2M24/RSV hIgG1
# Rituximab hIgG1
@ Isotype hIgG1

FIG. 36A

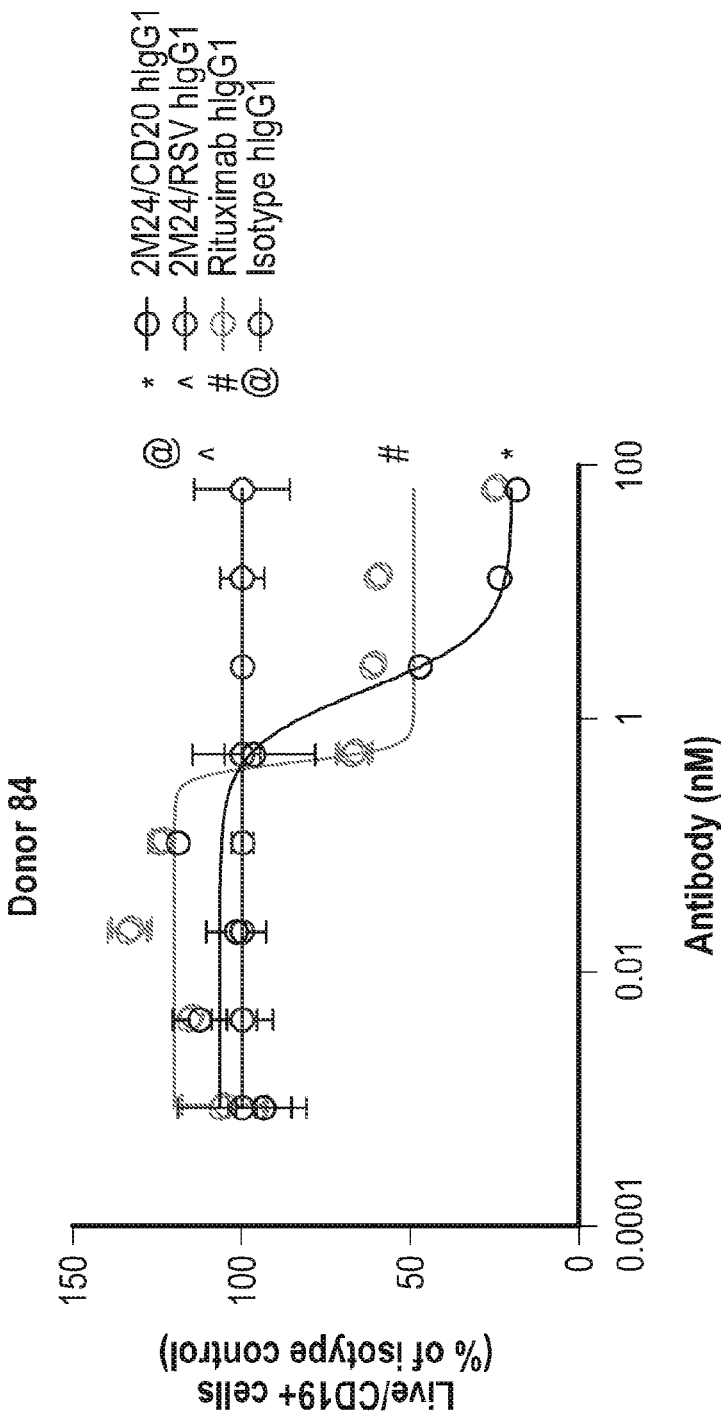

Donor 84
Live/CD19+ cells
(% of isotype control)
150
100
50
0
0.0001
0.01
1
100
Antibody (nM)
* 2M24/CD20 hIgG1
^ 2M24/RSV hIgG1
# Rituximab hIgG1
@ Isotype hIgG1

FIG. 36B

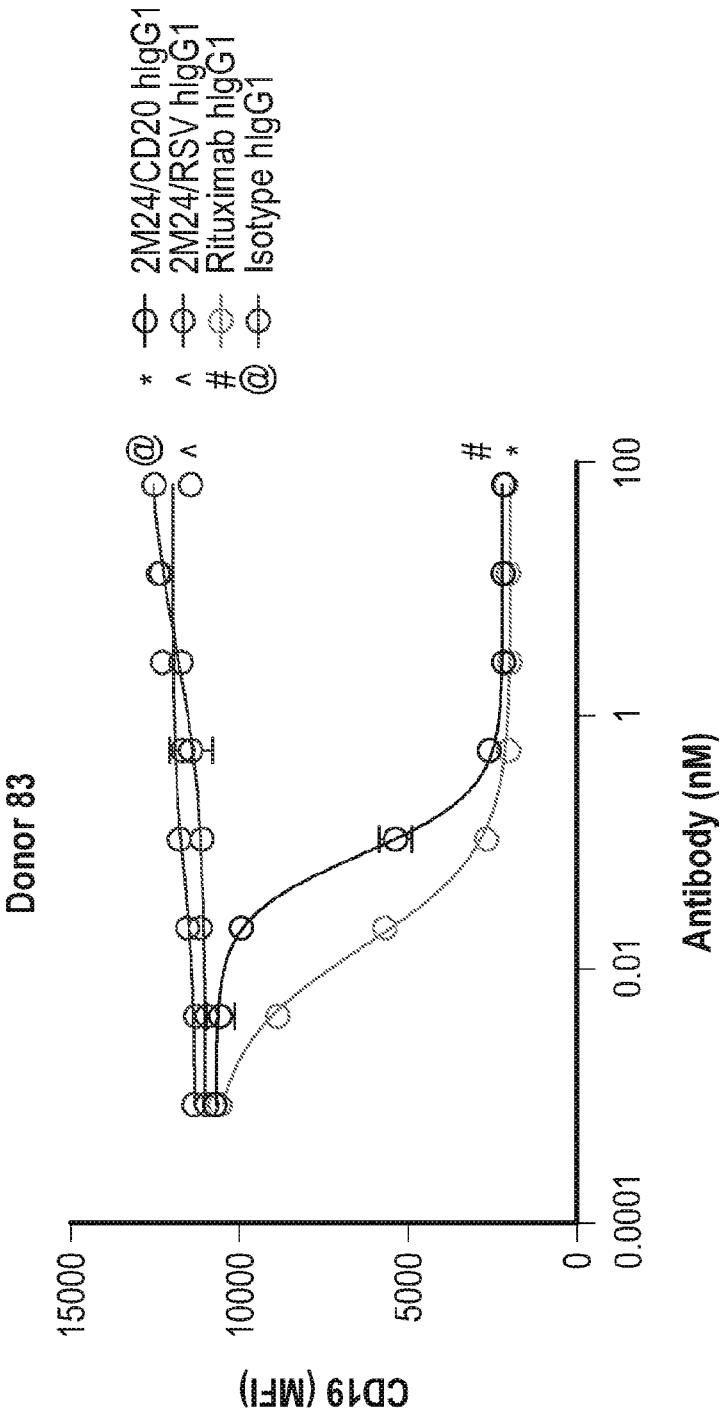

Donor 83
CD19 (MFI)
15000
10000
5000
0
0.0001
0.01
1
100
Antibody (nM)
* 2M24/CD20 hIgG1
^ 2M24/RSV hIgG1
# Rituximab hIgG1
@ Isotype hIgG1

FIG. 37A

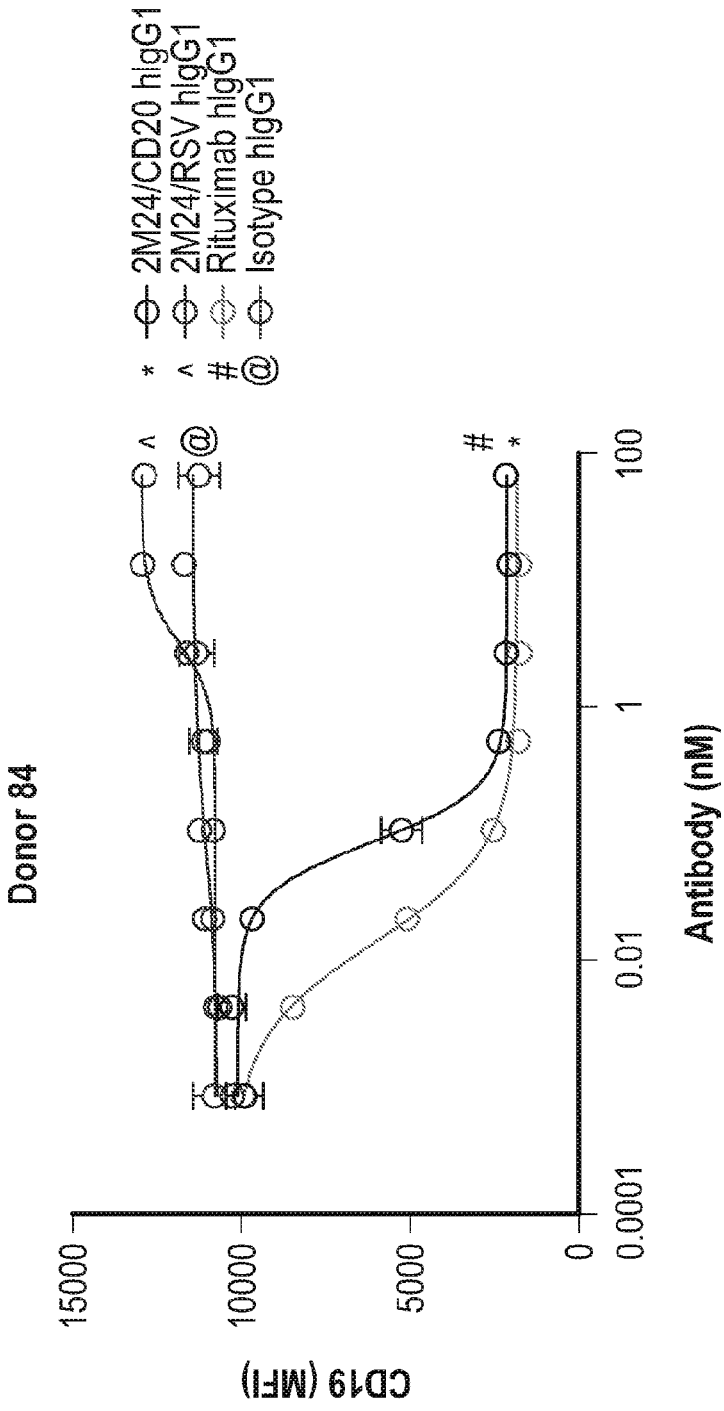

Donor 84
CD19 (MFI)
15000
10000
5000
0
0.0001
0.01
1
100
Antibody (nM)
* 2M24/CD20 hIgG1
^ 2M24/RSV hIgG1
# Rituximab hIgG1
@ Isotype hIgG1

FIG. 37B

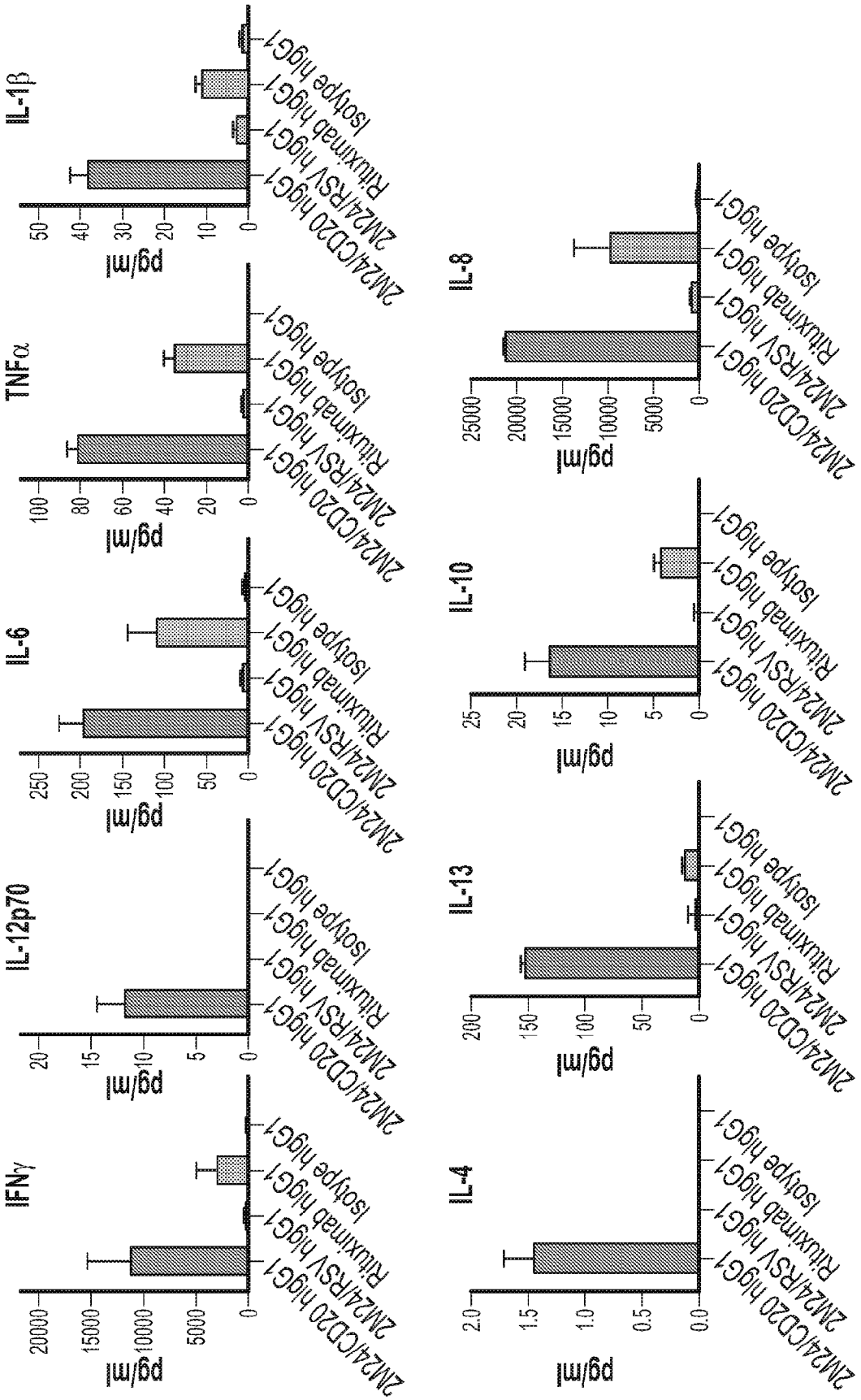

IFNγ
IL-12p70
IL-6
TNFα
IL-1β
IL-4
IL-13
IL-10
IL-8
pg/ml
2M24/CD20 hIgG1
2M24/RSV hIgG1
Rituximab hIgG1
Isotype hIgG1

FIG. 38

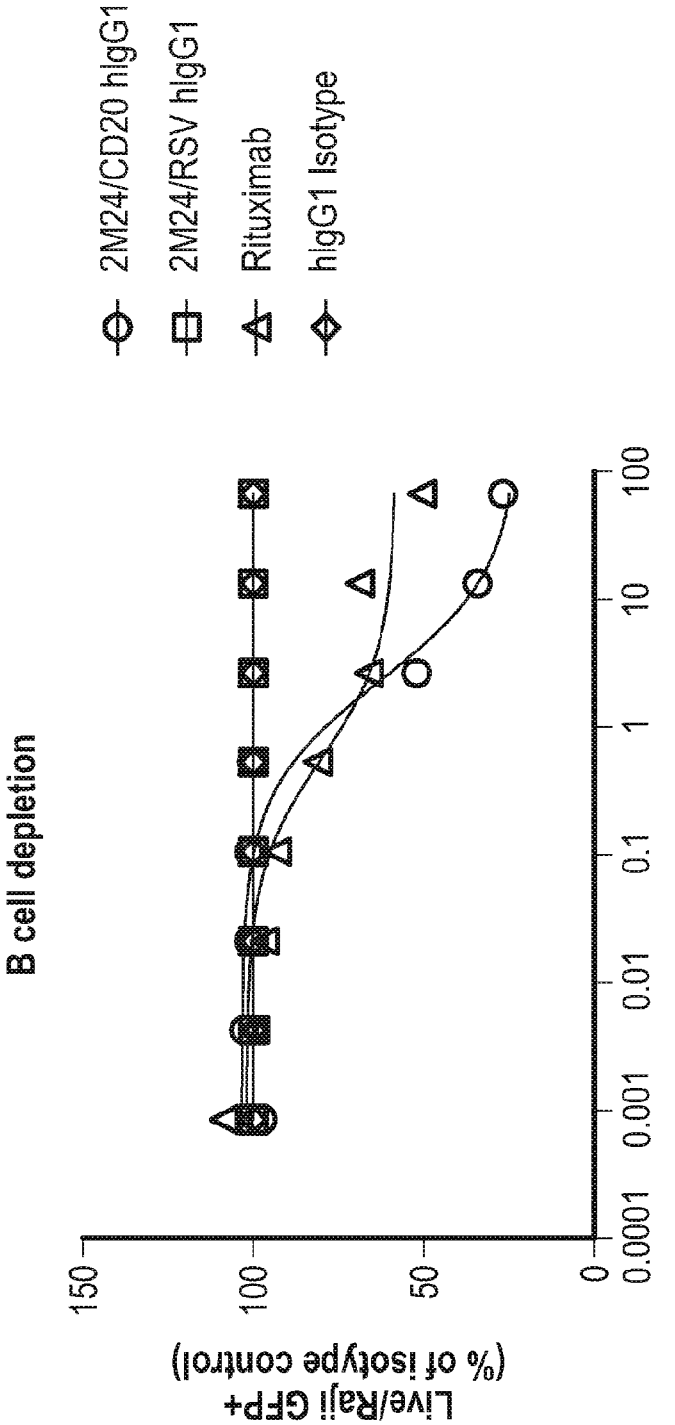

2M24/CD20 hIgG1
2M24/RSV hIgG1
Rituximab
hIgG1 Isotype
B cell depletion
Live/Raji GFP+
(% of isotype control)
150
100
50
0
0.0001
0.001
0.01
0.1
1
10
100
Concentration (nM)

FIG. 39A

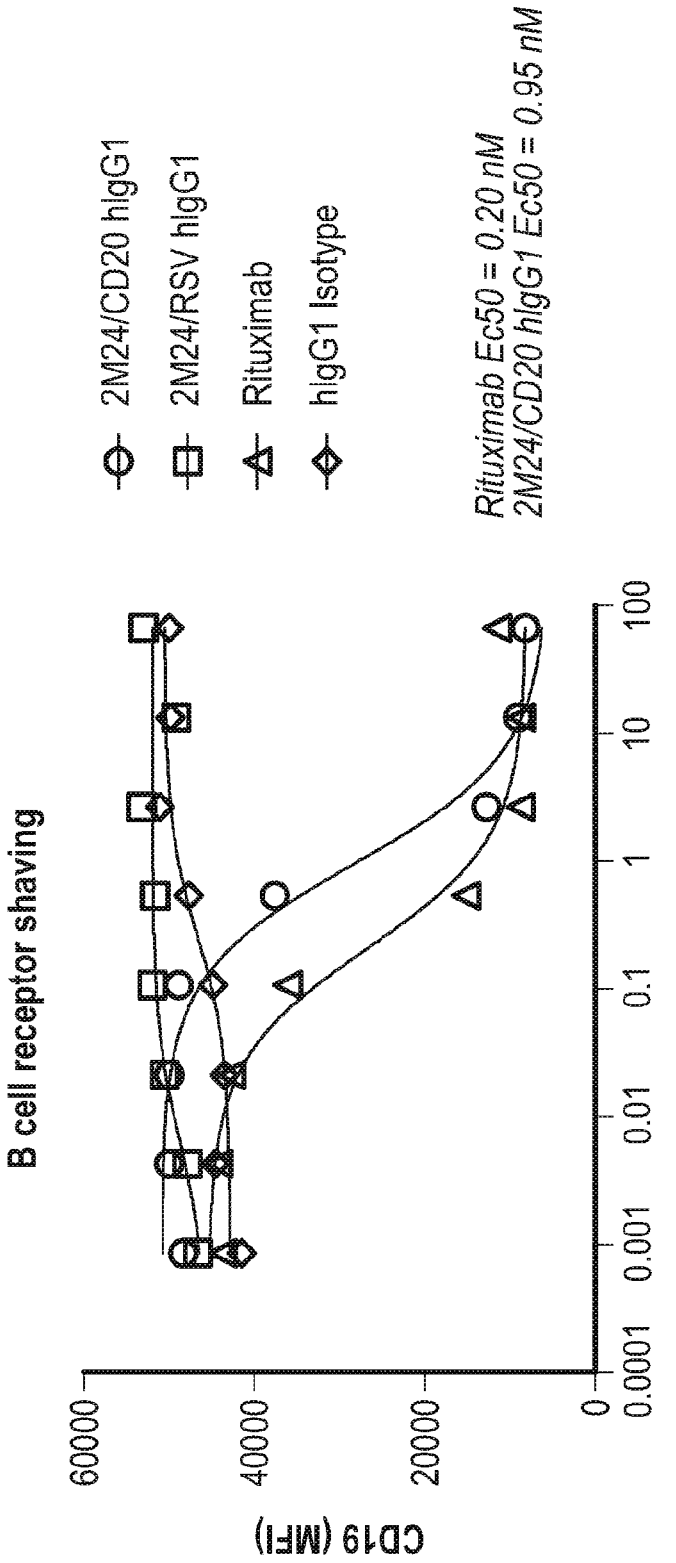

B cell receptor shaving
2M24/CD20 hIgG1
2M24/RSV hIgG1
Rituximab
hIgG1 Isotype
Rituximab Ec50 = 0.20 nM
2M24/CD20 hIgG1 Ec50 = 0.95 nM
CD19 (MFI)
60000
40000
20000
0
0.0001
0.001
0.01
0.1
1
10
100
Concentration (nM)

FIG. 39B

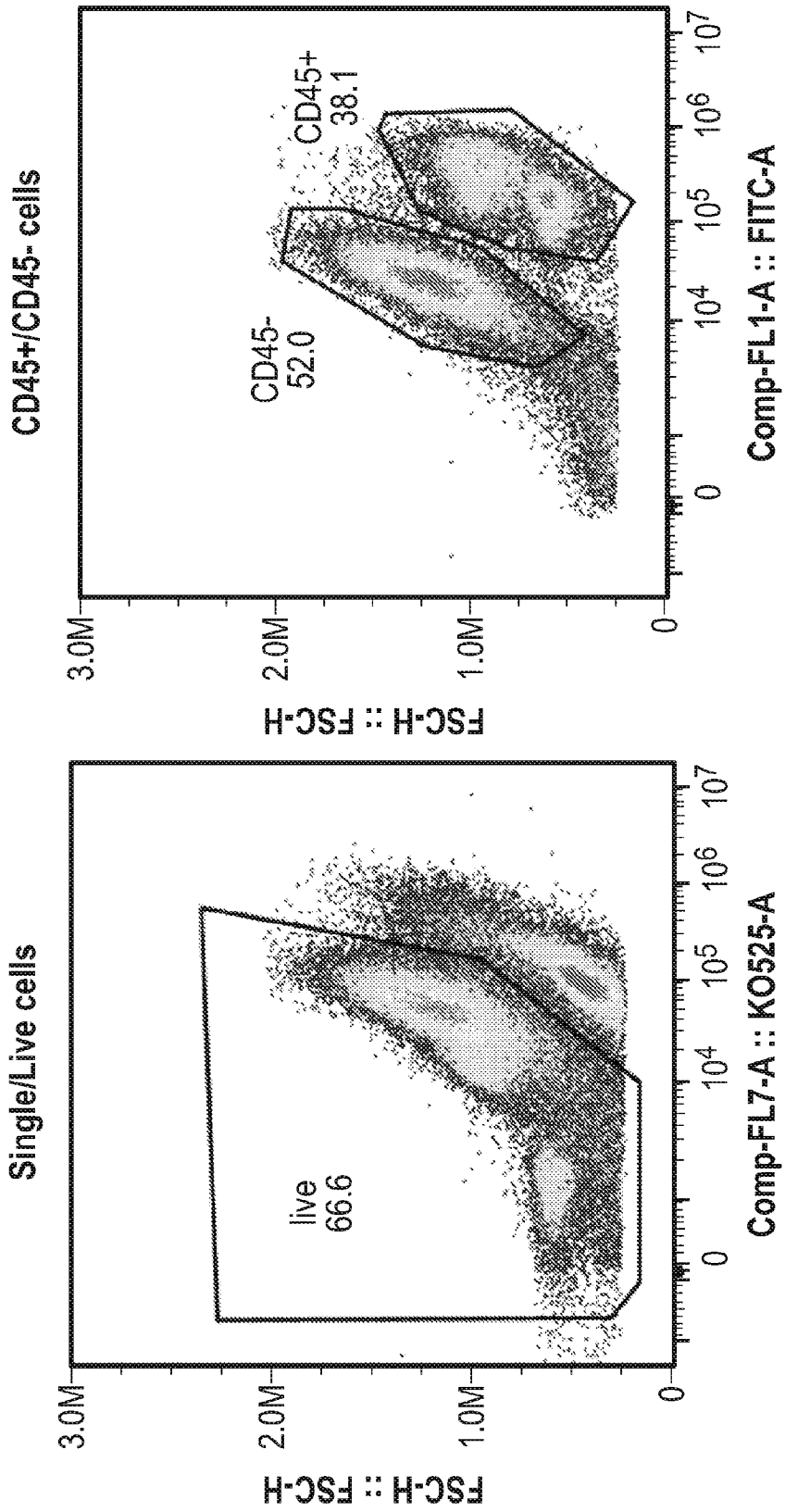

CD45+/CD45- cells
CD45+
38.1
CD45-
52.0
FSC-H :: FSC-H
3.0M
2.0M
1.0M
0
Comp-FL1-A :: FITC-A
Single/Live cells
live
66.6
Comp-FL7-A :: KO525-A

FIG. 40A

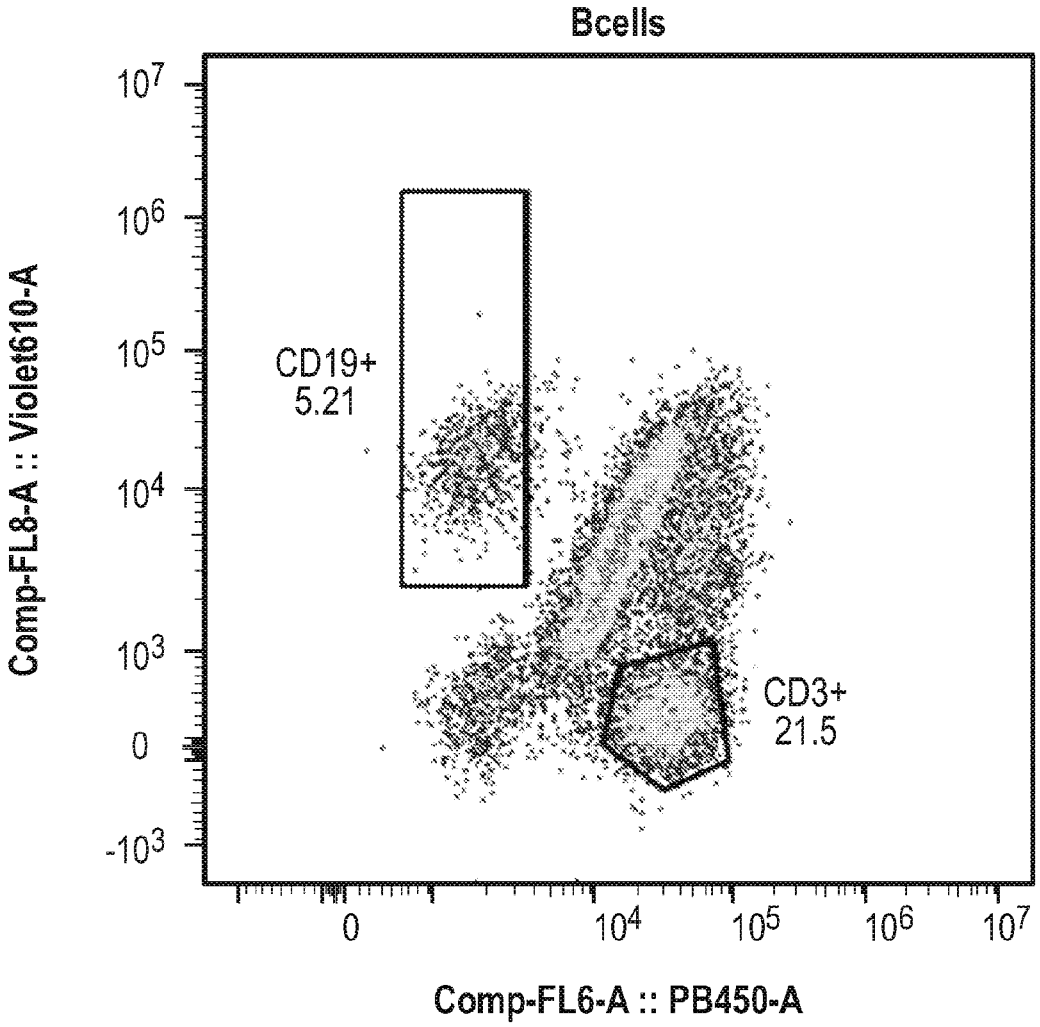

Bcells
CD19+
5.21
CD3+
21.5
Comp-FL8-A :: Violet610-A
Comp-FL6-A :: PB450-A
10^7
10^6
10^5
10^4
10^3
0
-10^3
0
10^4
10^5
10^6
10^7

FIG. 40B

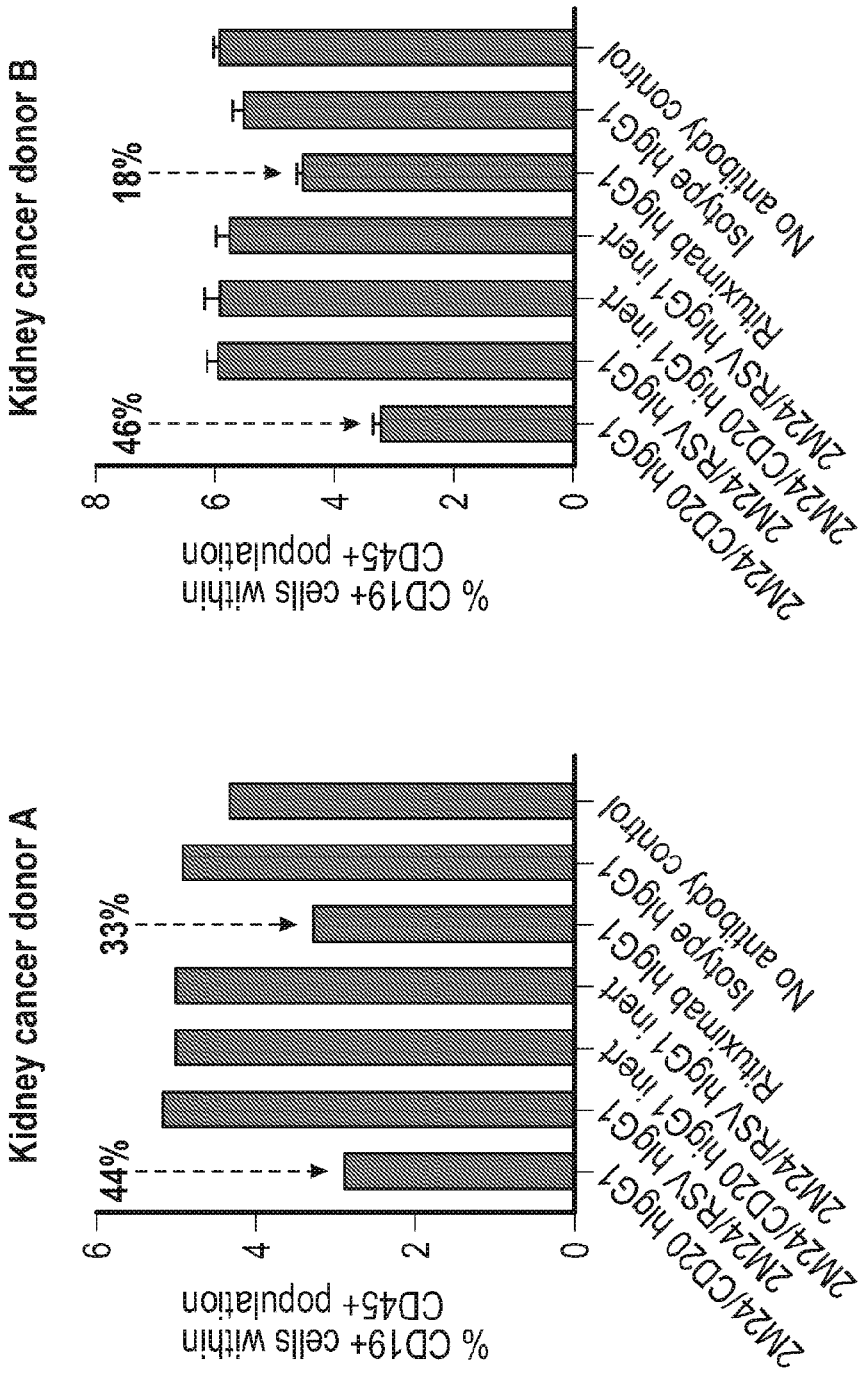

Kidney cancer donor A
% CD19+ cells within CD45+ population
0
2
4
6
44%
33%
2M24/CD20 hIgG1
2M24/RSV hIgG1
2M24/CD20 hIgG1 inert
2M24/RSV hIgG1 inert
Rituximab hIgG1
Isotype hIgG1
No antibody control
Kidney cancer donor B
% CD19+ cells within CD45+ population
0
2
4
6
8
46%
18%
2M24/CD20 hIgG1
2M24/RSV hIgG1
2M24/CD20 hIgG1 inert
2M24/RSV hIgG1 inert
Rituximab hIgG1
Isotype hIgG1
No antibody control

FIG. 40C

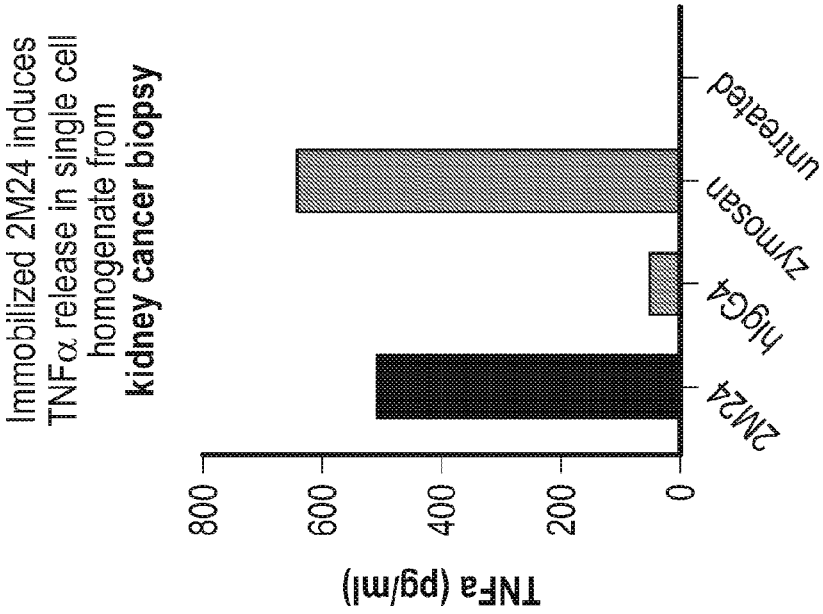


FIG. 41C

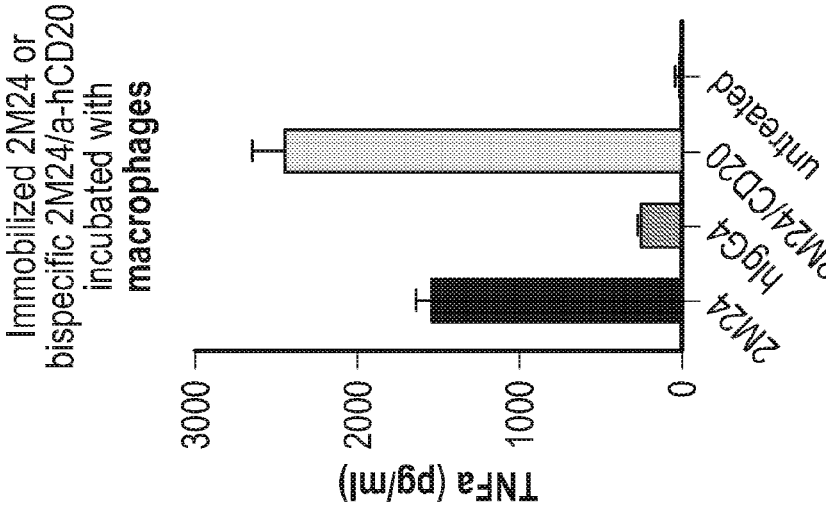


FIG. 41B

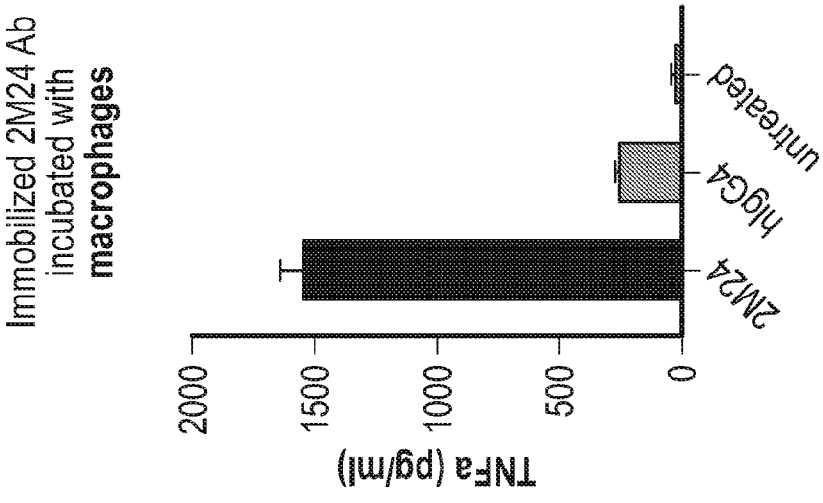


FIG. 41A

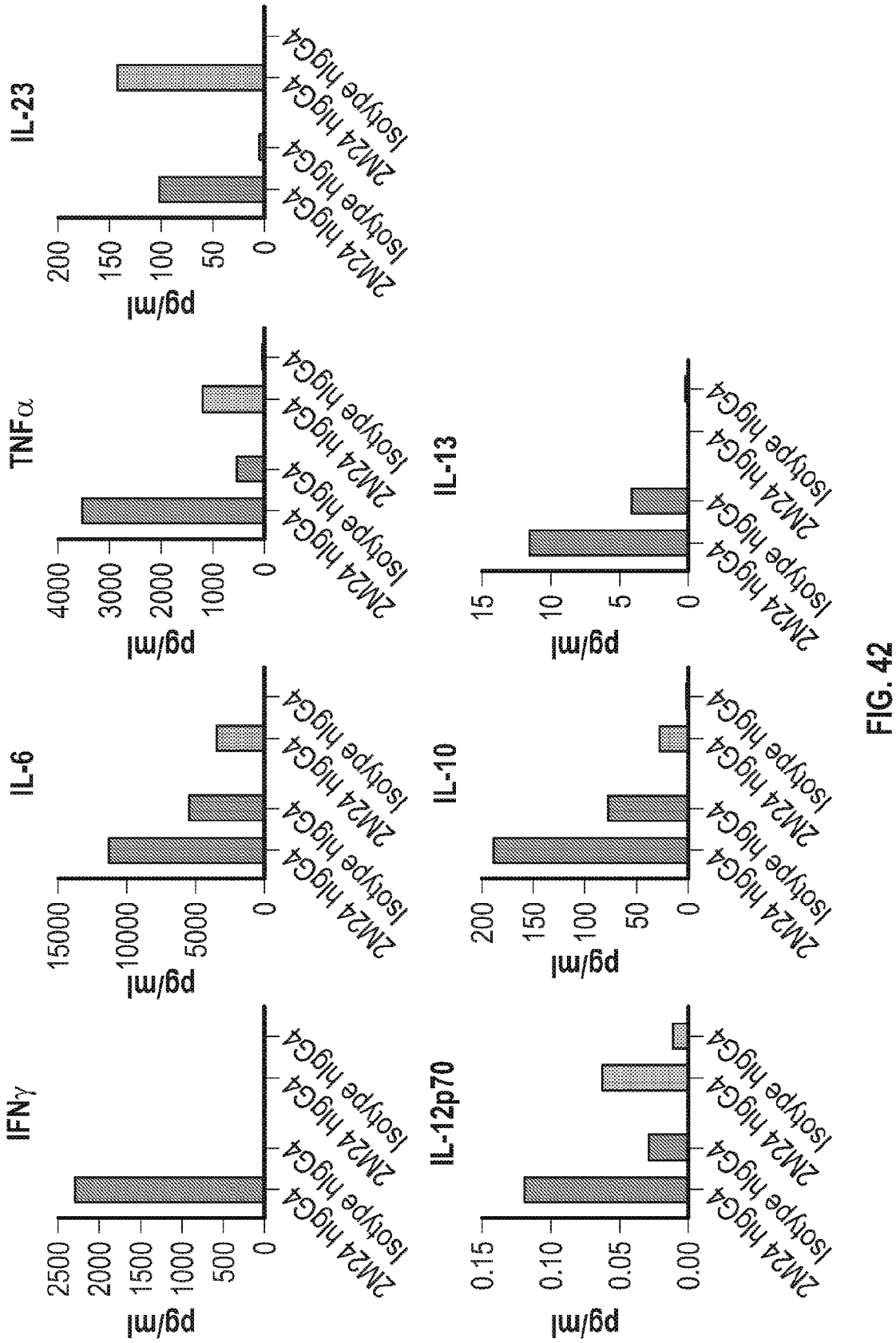

IL-23
TNFα
IL-13
IL-6
IL-10
IFNγ
IL-12p70
pg/ml
2M24 hIgG4
Isotype hIgG4

FIG. 42

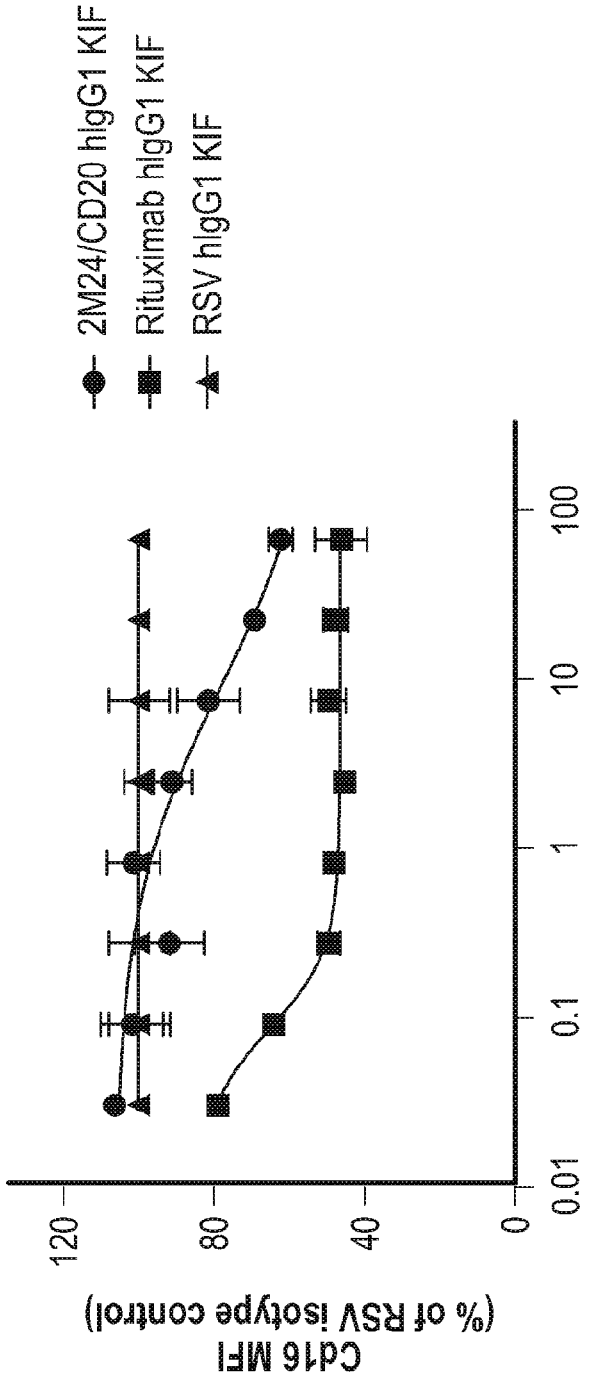

2M24/CD20 hIgG1 KIF
Rituximab hIgG1 KIF
RSV hIgG1 KIF
Cd16 MFI
(% of RSV isotype control)
120
80
40
0
0.01
0.1
1
10
100
Antibody (nM)

FIG. 43

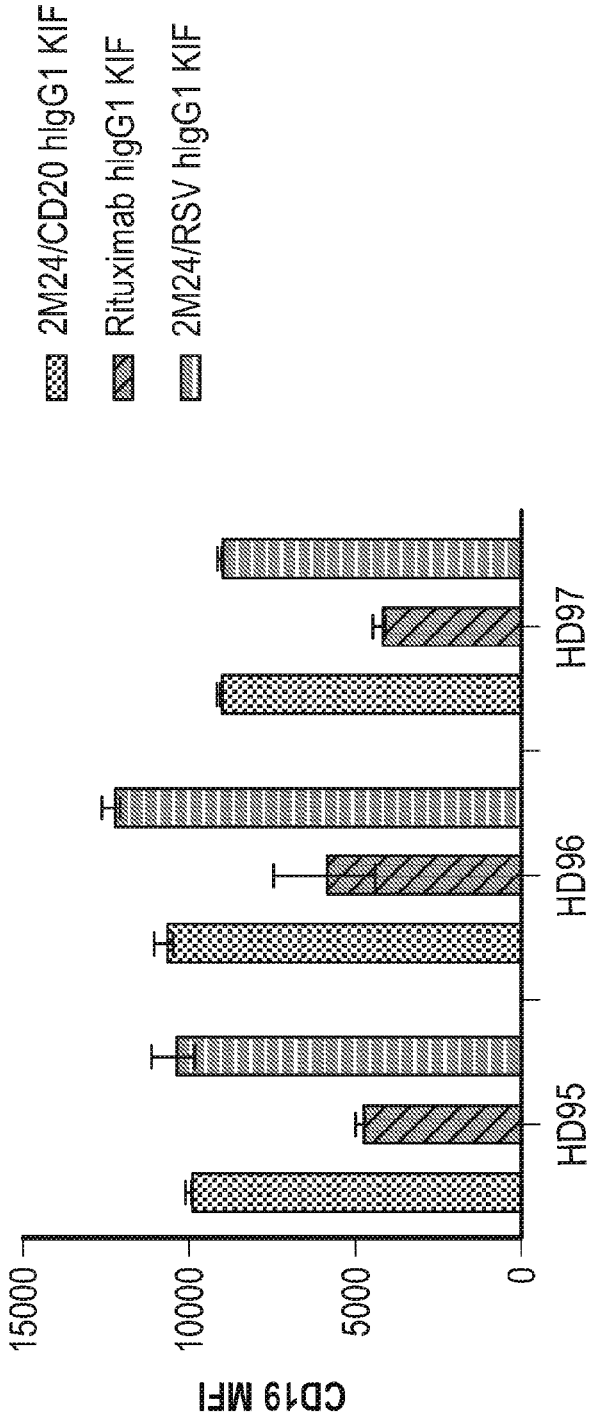

2M24/CD20 hIgG1 KIF
Rituximab hIgG1 KIF
2M24/RSV hIgG1 KIF
CD19 MFI
15000
10000
5000
0
HD95
HD96
HD97

FIG. 44

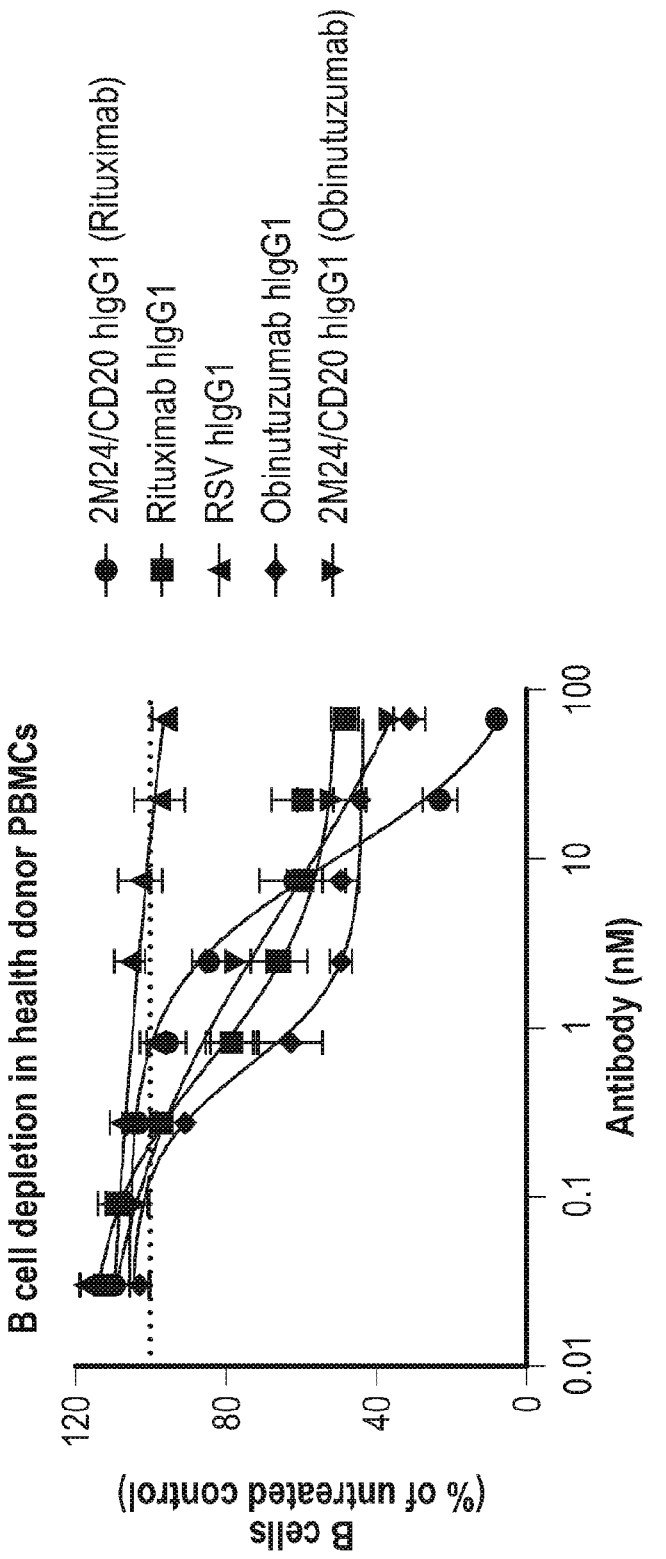

B cell depletion in health donor PBMCs
B cells
(% of untreated control)
120
80
40
0
0.01
0.1
1
10
100
Antibody (nM)
2M24/CD20 hIgG1 (Rituximab)
Rituximab hIgG1
RSV hIgG1
Obinutuzumab hIgG1
2M24/CD20 hIgG1 (Obinutuzumab)

FIG. 45

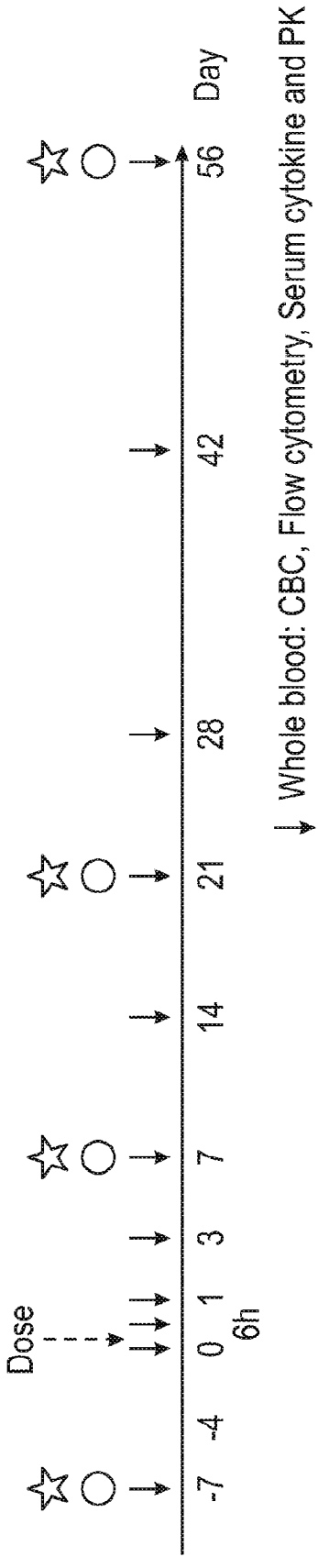
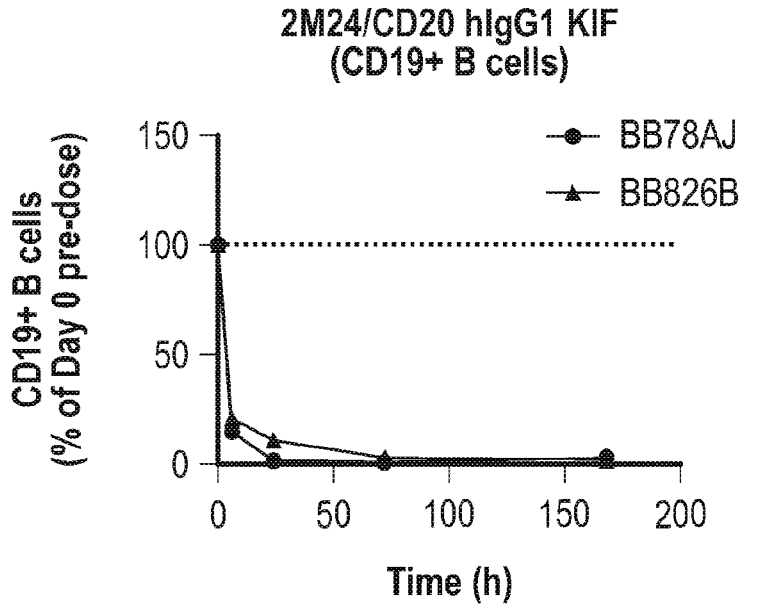

Day
-7
-4
0
1
6h
3
7
14
21
28
42
56
Dose
Whole blood: CBC, Flow cytometry, Serum cytokine and PK
Tissue collection: BM, LN, colorectal tissue
Whole blood: Chemistry, Coagulation

FIG. 46


2M24/CD20 hIgG1 KIF
(CD19+ B cells)
CD19+ B cells
(% of Day 0 pre-dose)
150
100
50
0
0
50
100
150
200
Time (h)
BB78AJ
BB826B

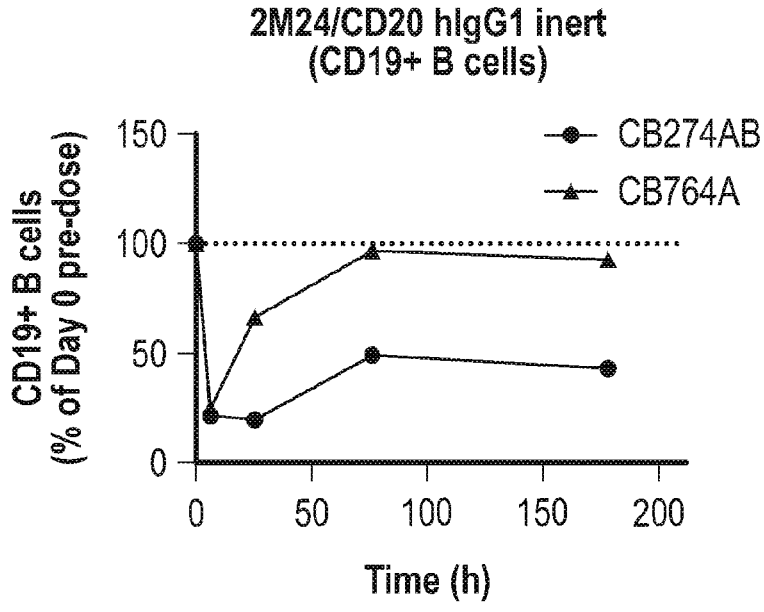

2M24/CD20 hIgG1 inert
(CD19+ B cells)
CD19+ B cells
(% of Day 0 pre-dose)
150
100
50
0
0
50
100
150
200
Time (h)
CB274AB
CB764A

FIG. 47

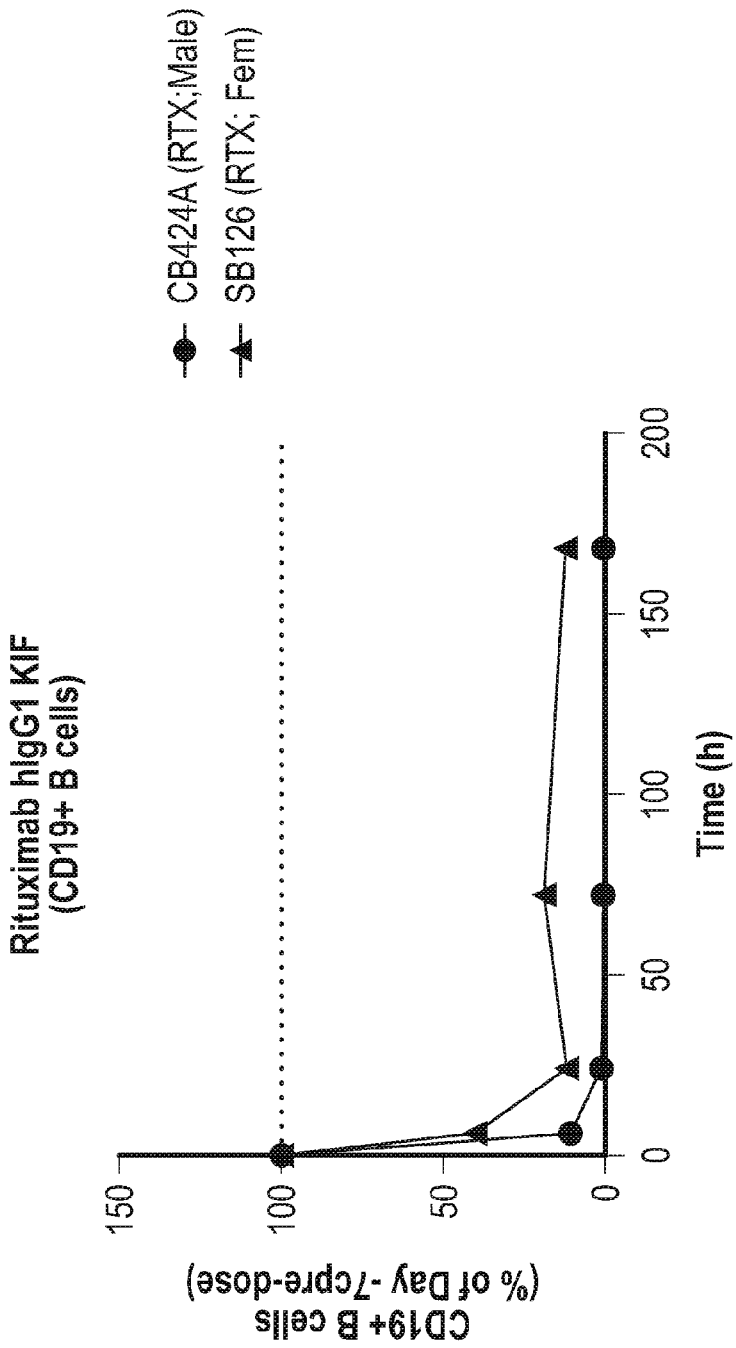

Rituximab hIgG1 KIF
(CD19+ B cells)
CB424A (RTX;Male)
SB126 (RTX; Fem)
CD19+ B cells
(% of Day -7pre-dose)
150
100
50
0
0
50
100
150
200
Time (h)

FIG. 48

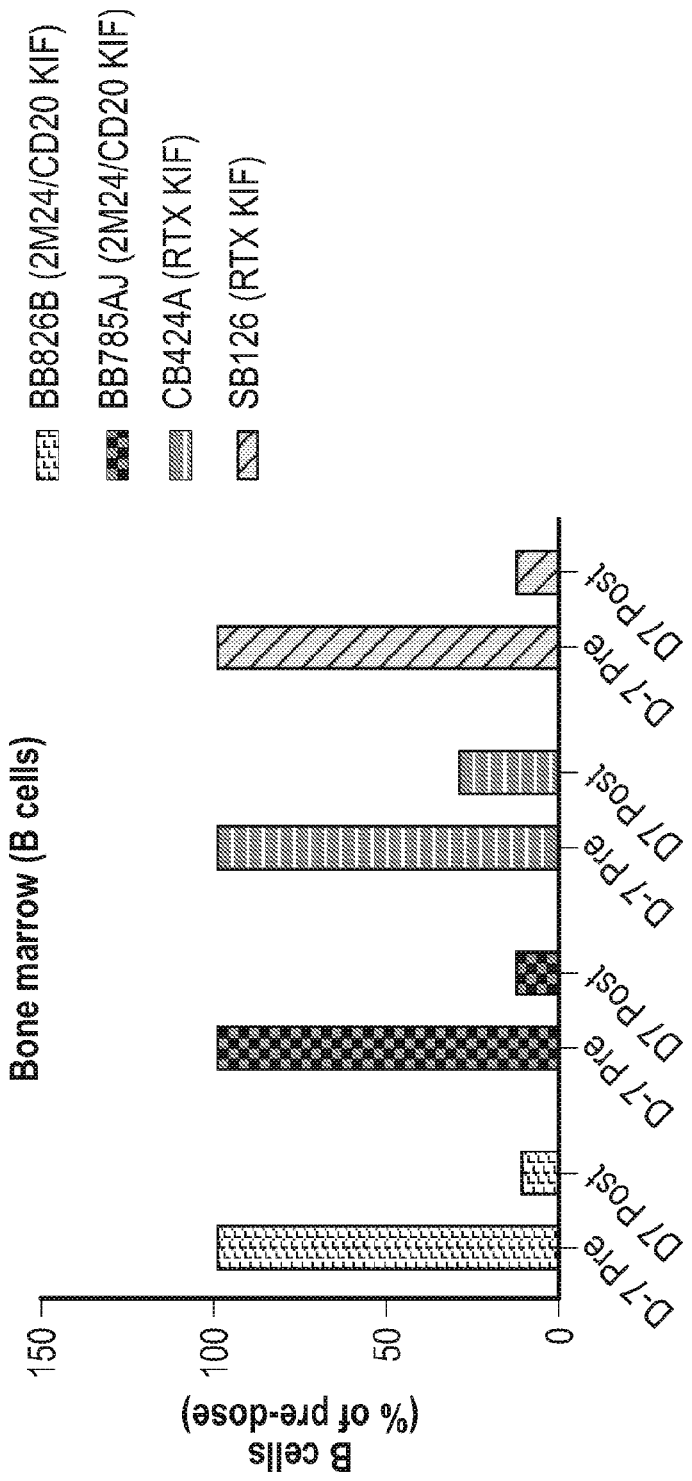

BB826B (2M24/CD20 KIF)
BB785AJ (2M24/CD20 KIF)
CB424A (RTX KIF)
SB126 (RTX KIF)
Bone marrow (B cells)
B cells
(% of pre-dose)
150
100
50
0
D-7 Pre
D7 Post
D-7 Pre
D7 Post
D-7 Pre
D7 Post
D-7 Pre
D7 Post

FIG. 49A

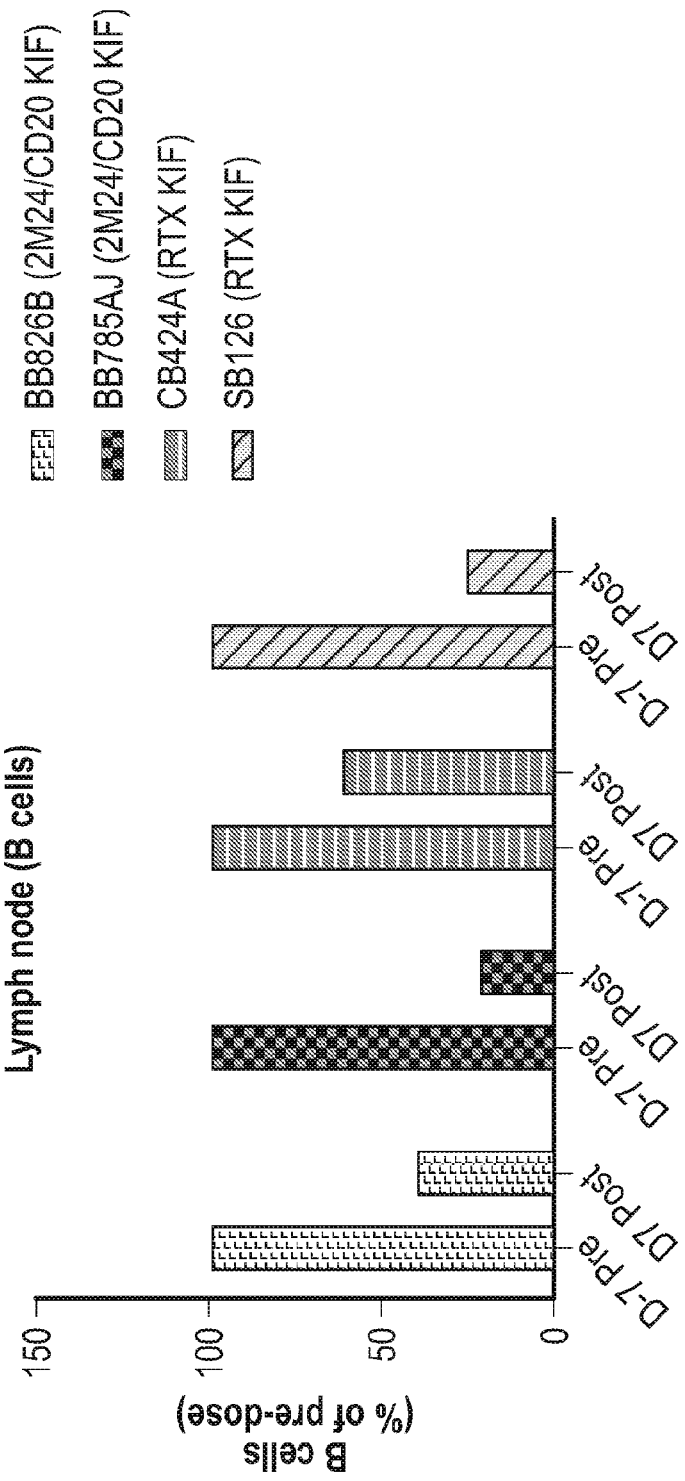

BB826B (2M24/CD20 KIF)
BB785AJ (2M24/CD20 KIF)
CB424A (RTX KIF)
SB126 (RTX KIF)
Lymph node (B cells)
B cells
(% of pre-dose)
150
100
50
0
D-7 Pre
D7 Post
D-7 Pre
D7 Post
D-7 Pre
D7 Post
D-7 Pre
D7 Post

FIG. 49B

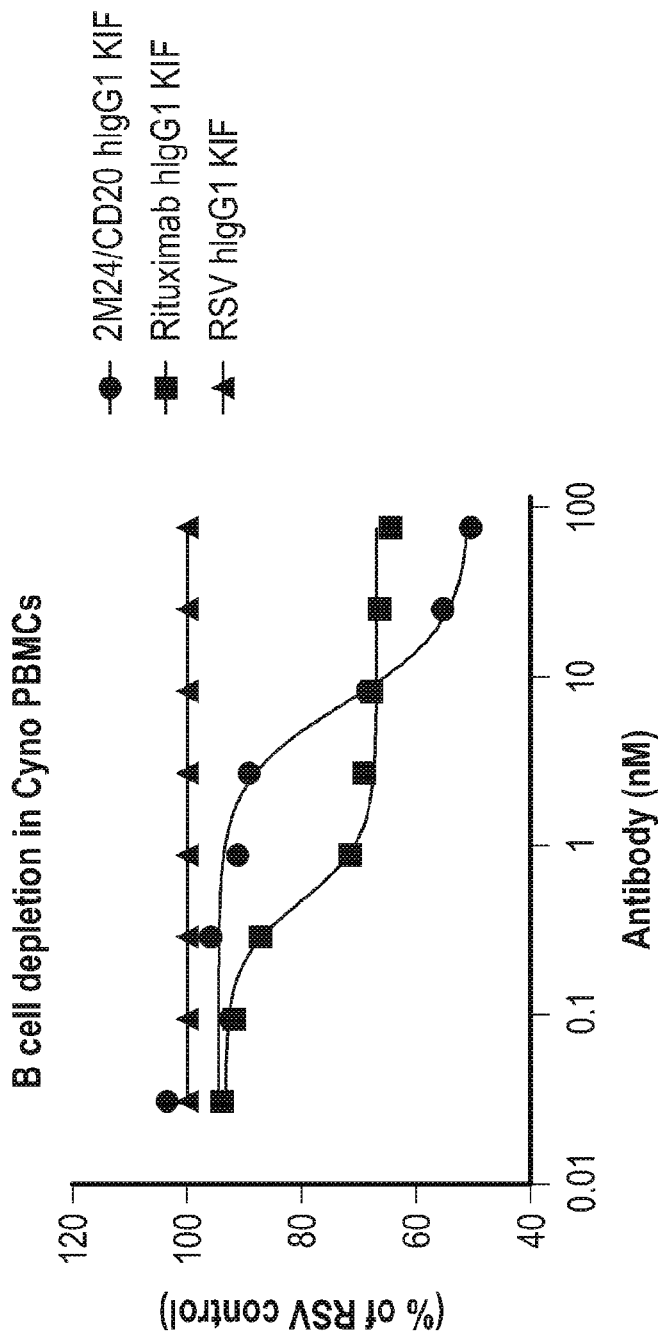

B cell depletion in Cyno PBMCs
2M24/CD20 hIgG1 KIF
Rituximab hIgG1 KIF
RSV hIgG1 KIF
(% of RSV control)
120
100
80
60
40
0.01
0.1
1
10
100
Antibody (nM)

FIG. 50

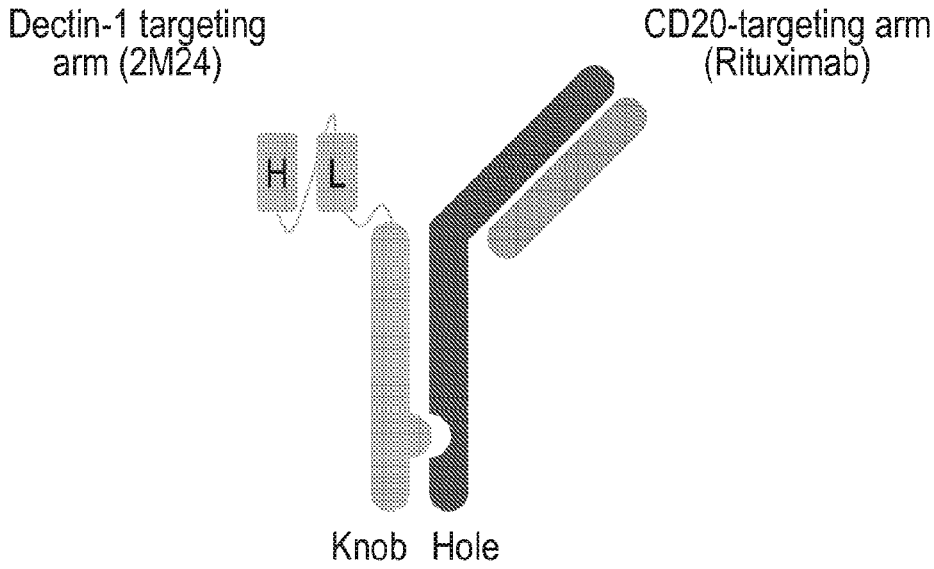

Dectin-1 targeting arm (2M24)
CD20-targeting arm (Rituximab)
H
L
Knob
Hole
hIgG1

FIG. 51

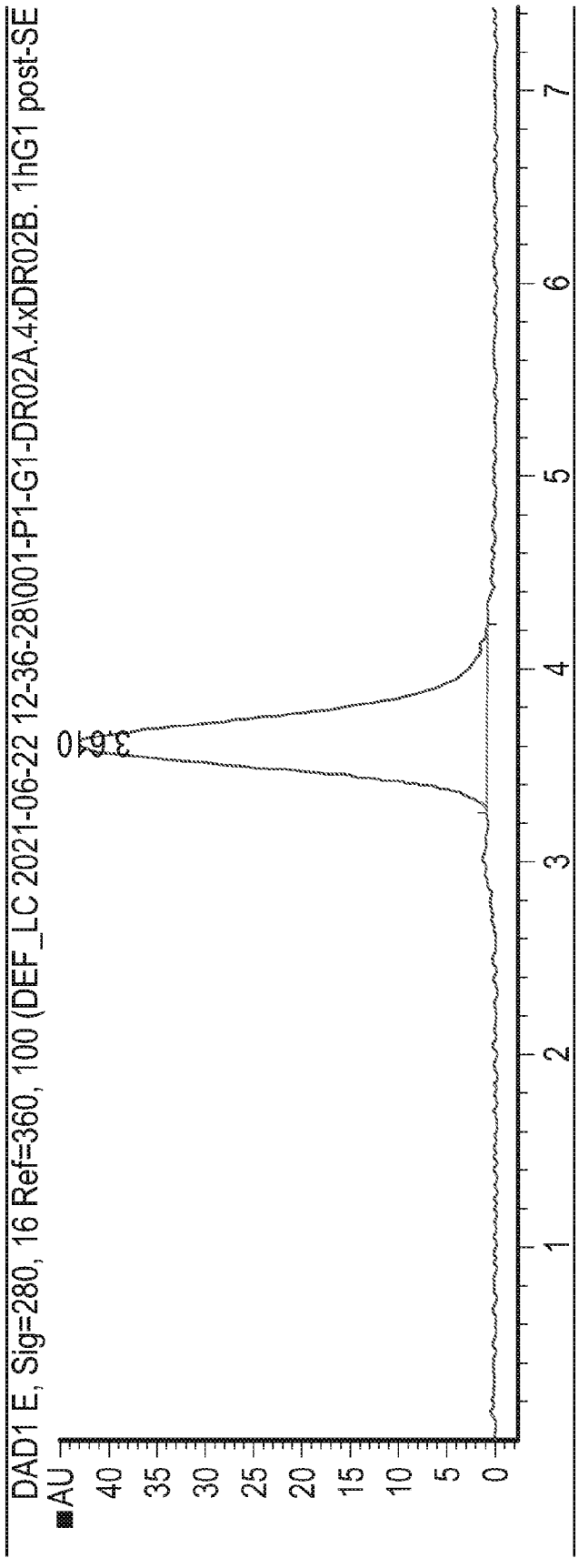

DAD1 E, Sig=280, 16 Ref=360, 100 (DEF_LC 2021-06-22 12-36-28\001-P1-G1-DR02A.4xDR02B. 1hG1 post-SE
AU
40
35
30
25
20
15
10
5
0
1
2
3
4
5
6
7
Time (min)

FIG. 52A

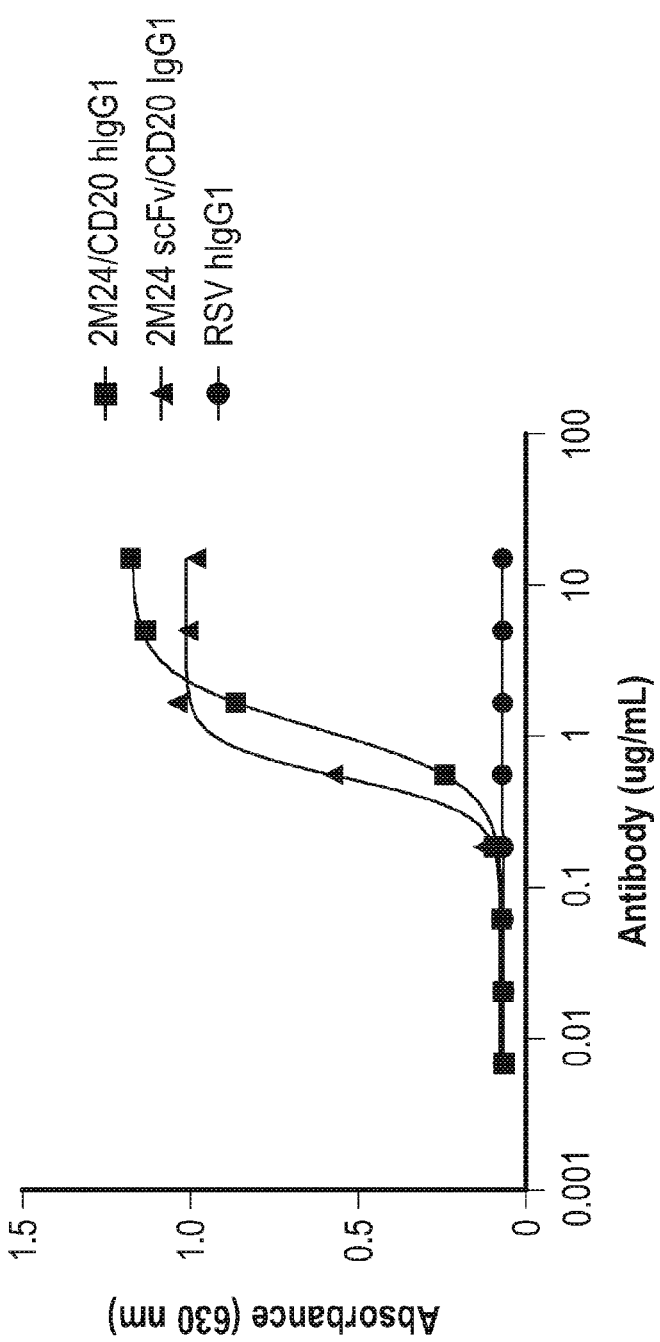

2M24/CD20 hIgG1
2M24 scFv/CD20 IgG1
RSV hIgG1
Absorbance (630 nm)
1.5
1.0
0.5
0
0.001
0.01
0.1
1
10
100
Antibody (ug/mL)

FIG. 52B

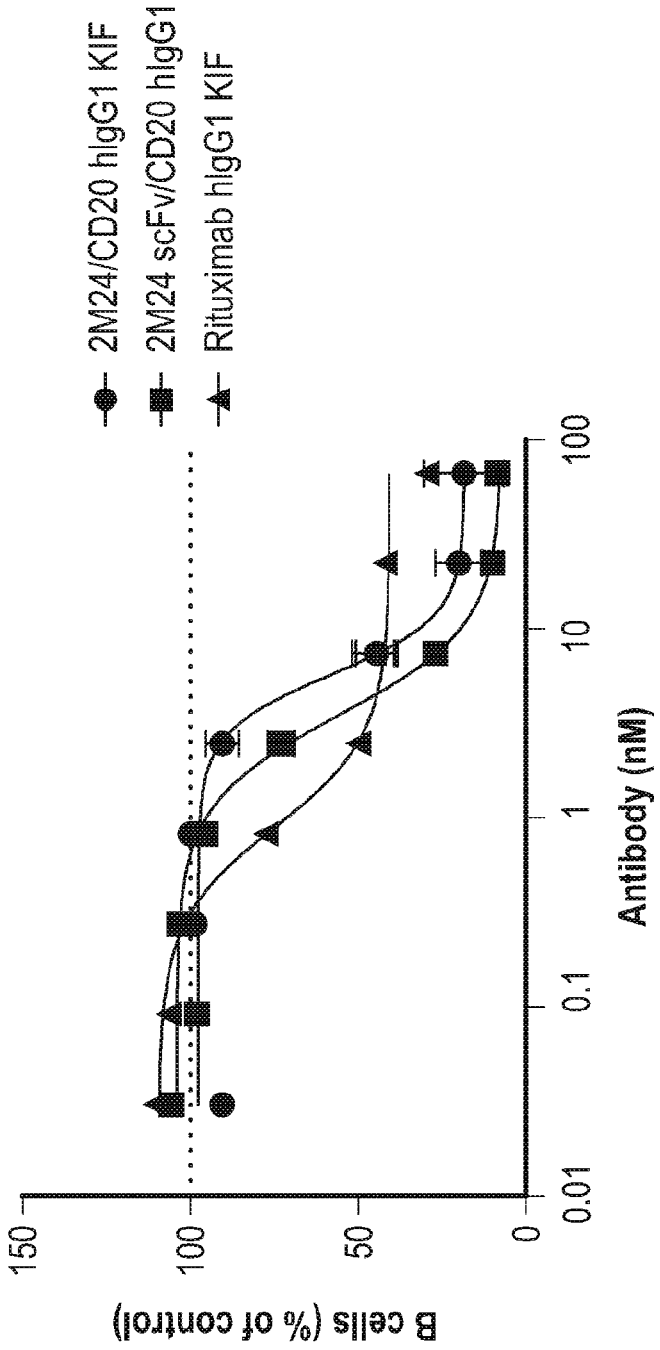

2M24/CD20 hIgG1 KIF
2M24 scFv/CD20 hIgG1
Rituximab hIgG1 KIF
B cells (% of control)
150
100
50
0
0.01
0.1
1
10
100
Antibody (nM)

FIG. 52C

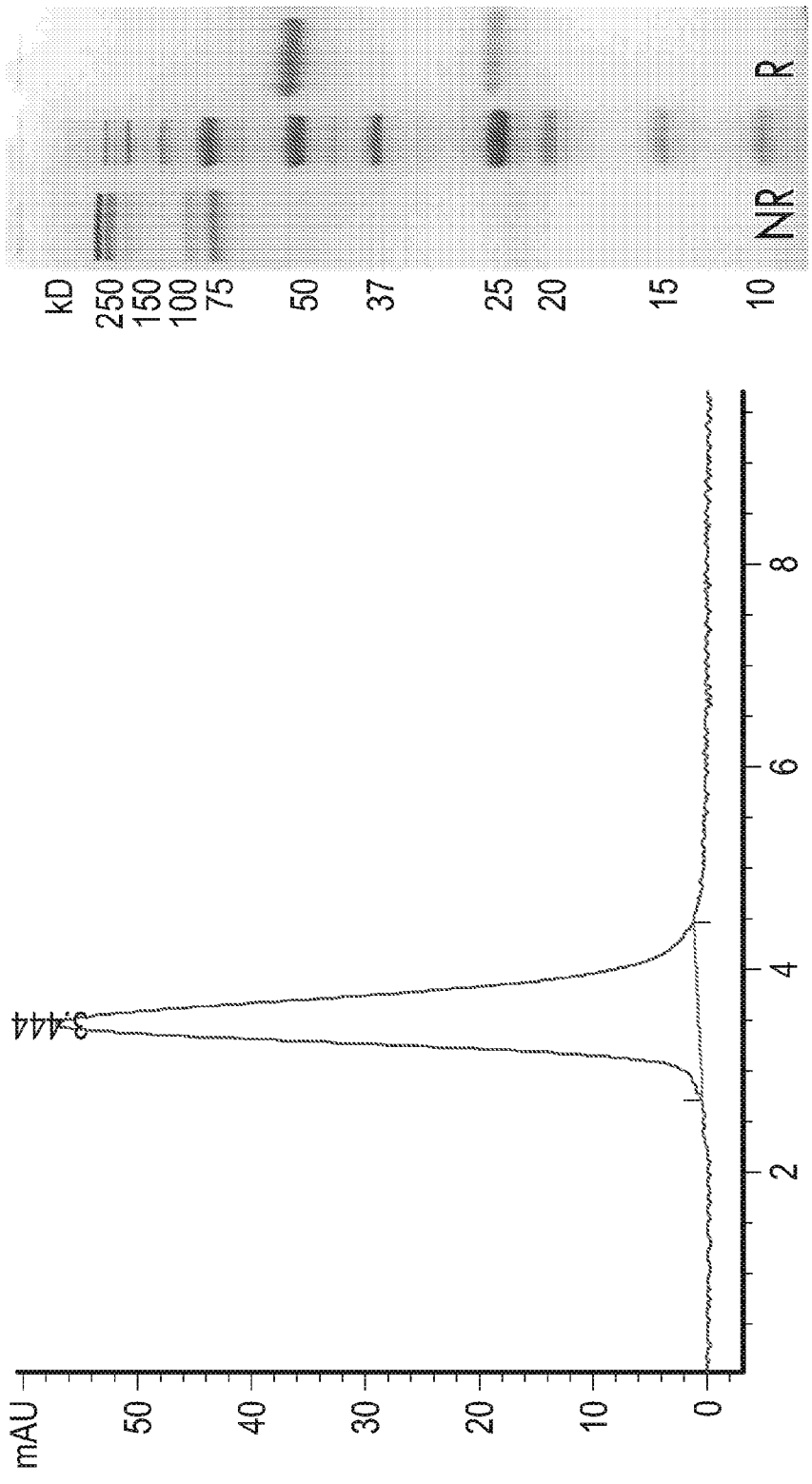

kD
250
150
100
75
50
37
25
20
15
10
NR
R
mAU
50
40
30
20
10
0
3.444
2
4
6
8

FIG. 53A

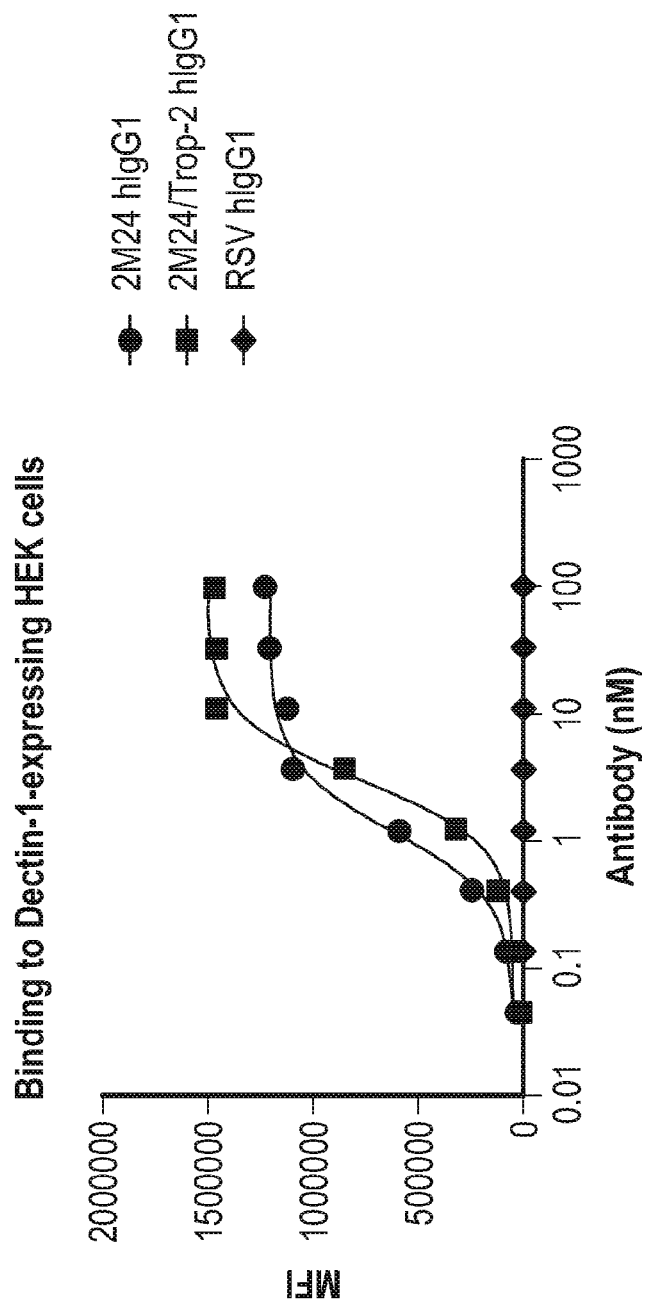

Binding to Dectin-1-expressing HEK cells
2M24 hIgG1
2M24/Trop-2 hIgG1
RSV hIgG1
MFI
2000000
1500000
1000000
500000
0
0.01
0.1
1
10
100
1000
Antibody (nM)

FIG. 53B

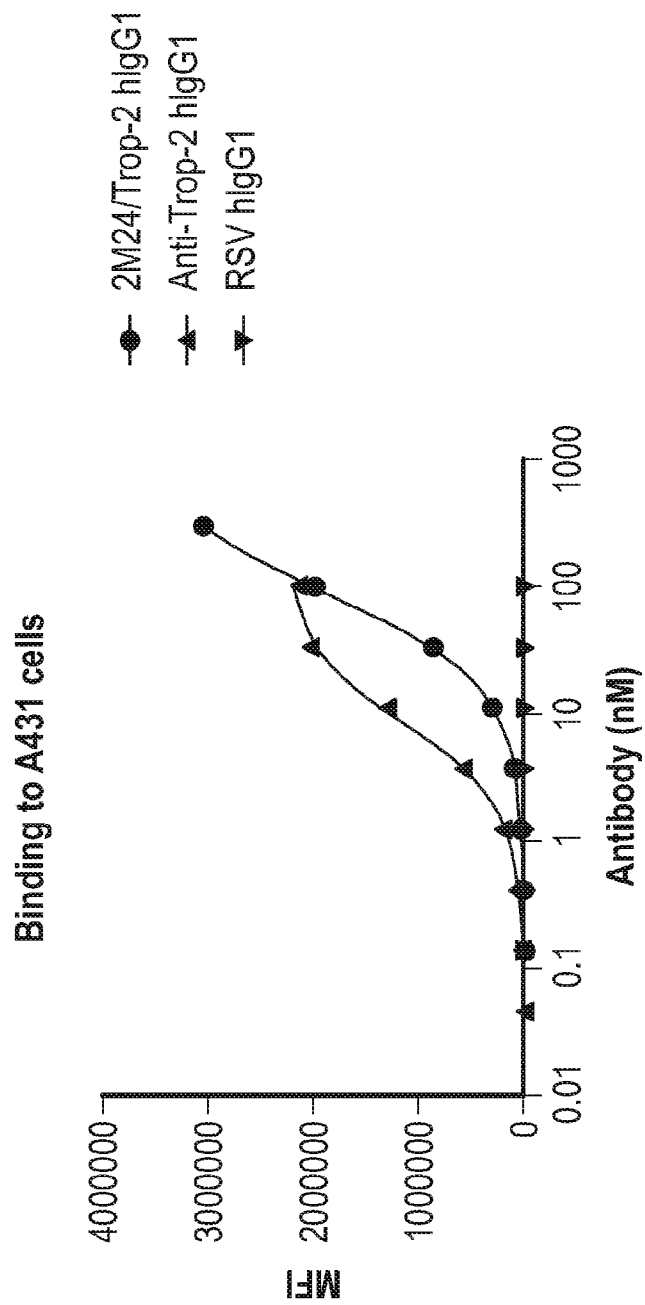

Binding to A431 cells
2M24/Trop-2 hIgG1
Anti-Trop-2 hIgG1
RSV hIgG1
MFI
4000000
3000000
2000000
1000000
0
0.01
0.1
1
10
100
1000
Antibody (nM)

FIG. 53C

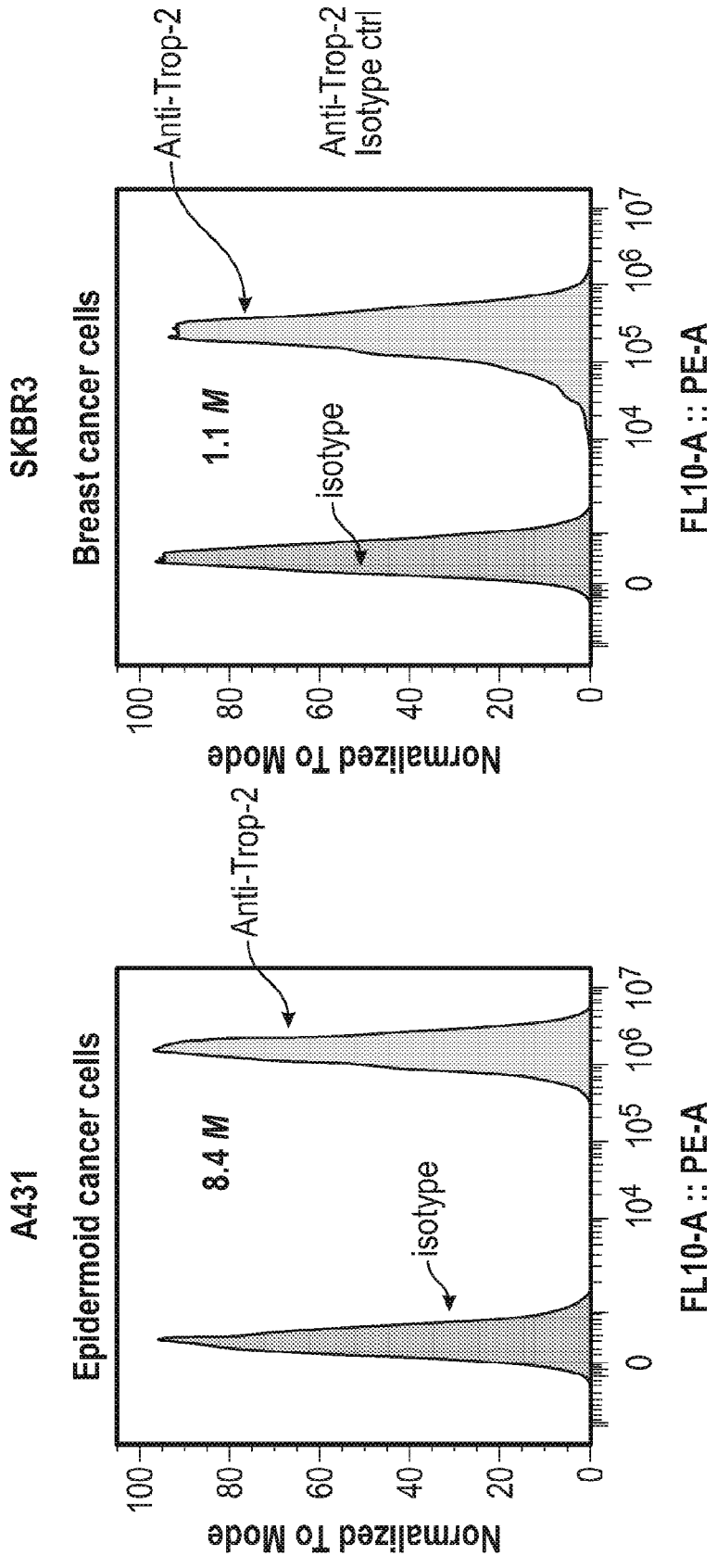

SKBR3
Breast cancer cells
Anti-Trop-2
Anti-Trop-2
Isotype ctrl
1.1 M
isotype
Normalized To Mode
FL10-A :: PE-A
A431
Epidermoid cancer cells
Anti-Trop-2
8.4 M
isotype
Normalized To Mode
FL10-A :: PE-A

FIG. 54

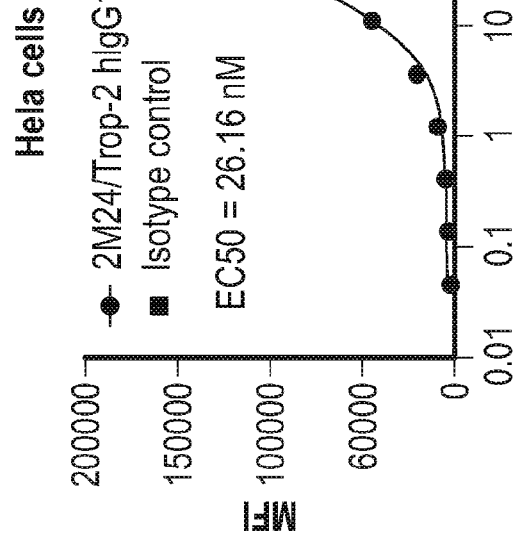


FIG. 55A

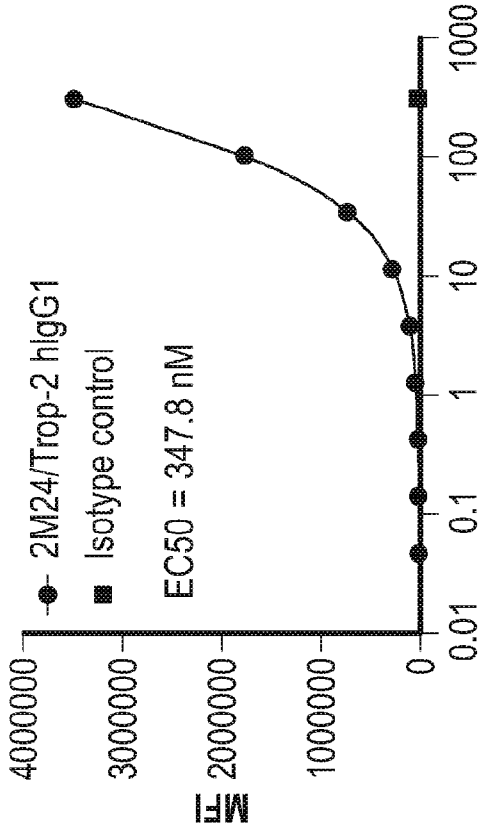


FIG. 55B

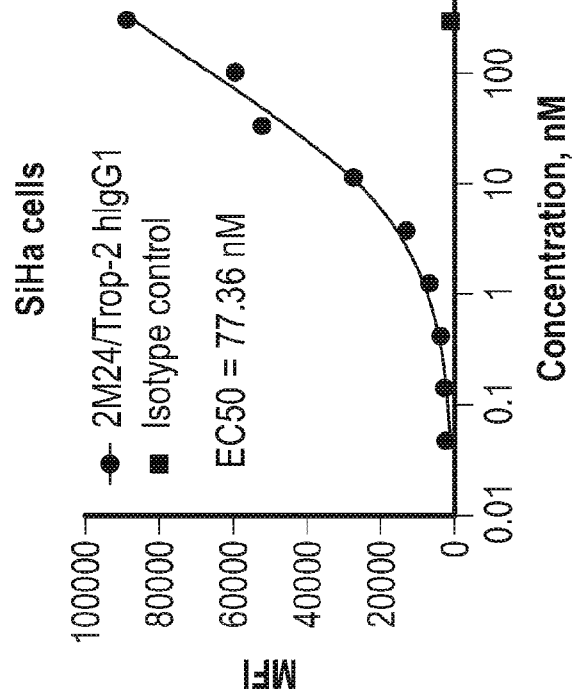


FIG. 55C

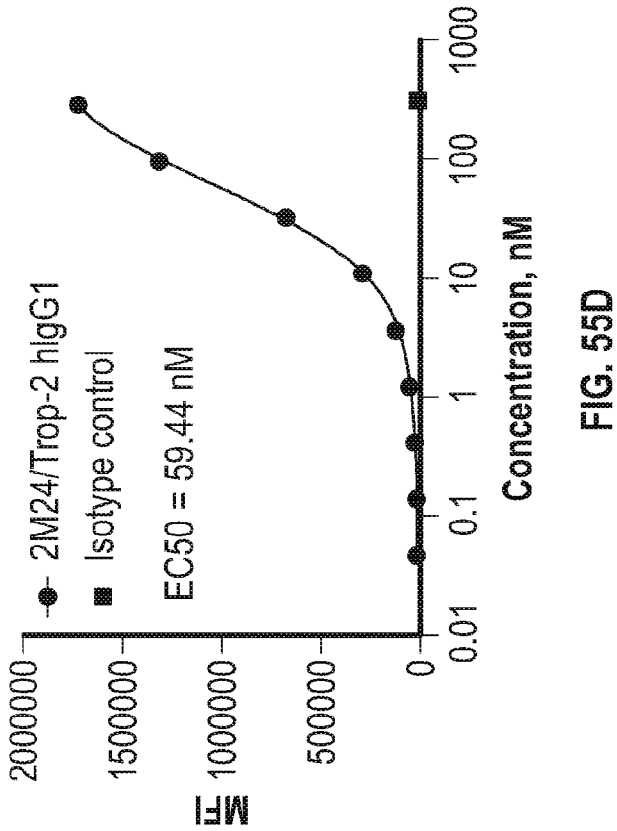


FIG. 55D

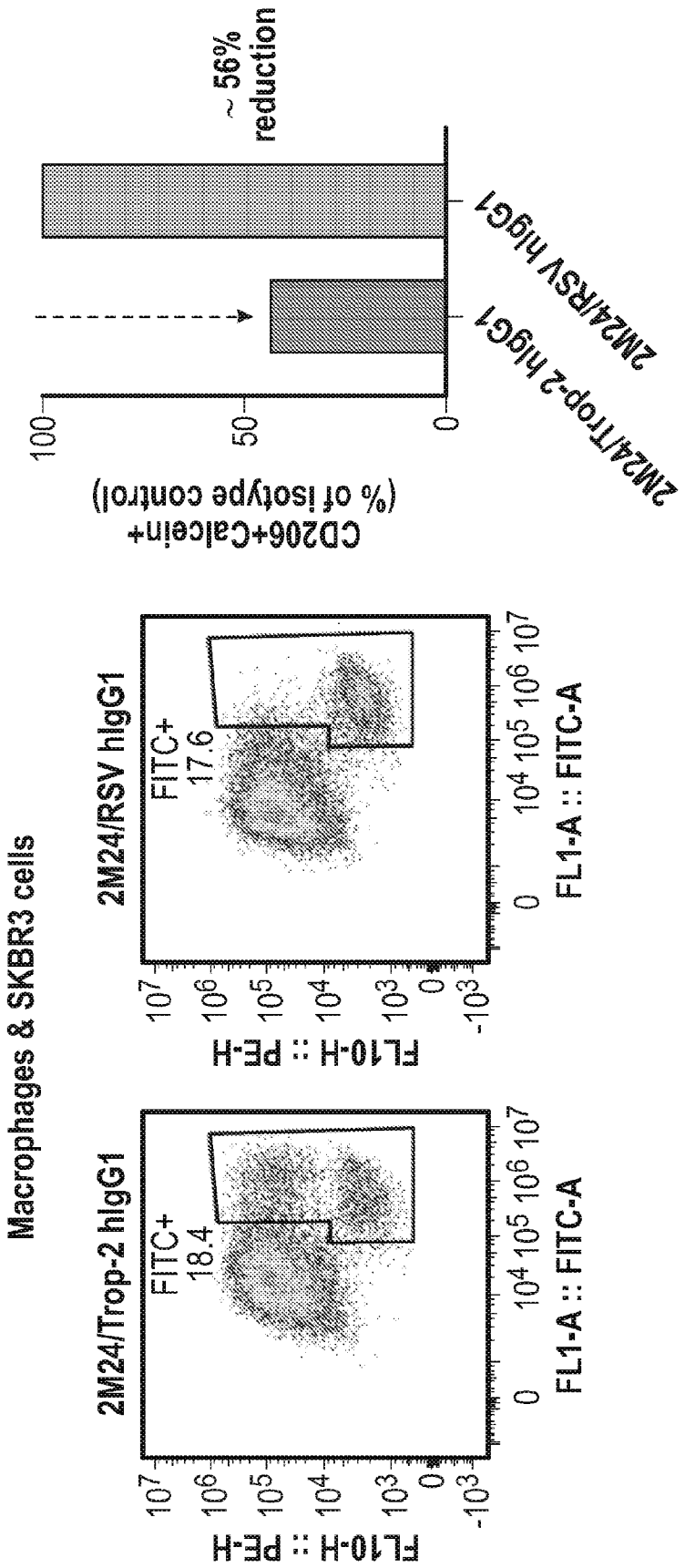

Macrophages & SKBR3 cells
2M24/Trop-2 hIgG1
FITC+
18.4
2M24/RSV hIgG1
FITC+
17.6
FL10-H :: PE-H
FL1-A :: FITC-A
CD206+Calcein+
(% of isotype control)
100
50
0
~ 56%
reduction
2M24/Trop-2 hIgG1
2M24/RSV hIgG1

FIG. 56A

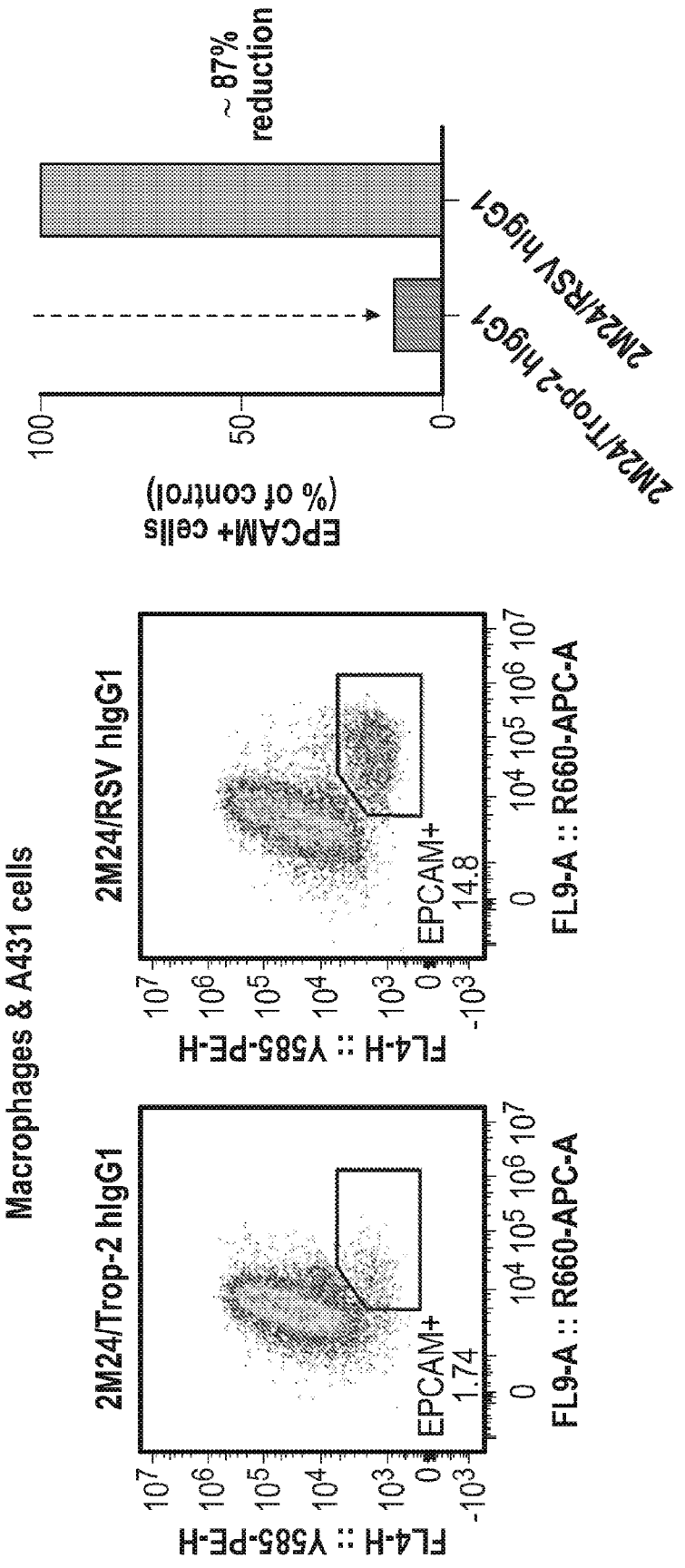

Macrophages & A431 cells
2M24/Trop-2 hIgG1
2M24/RSV hIgG1
FL4-H :: Y585-PE-H
FL9-A :: R660-APC-A
EPCAM+
1.74
14.8
EPCAM+ cells
(% of control)
100
50
0
~ 87%
reduction
2M24/Trop-2 hIgG1
2M24/RSV hIgG1

FIG. 56B

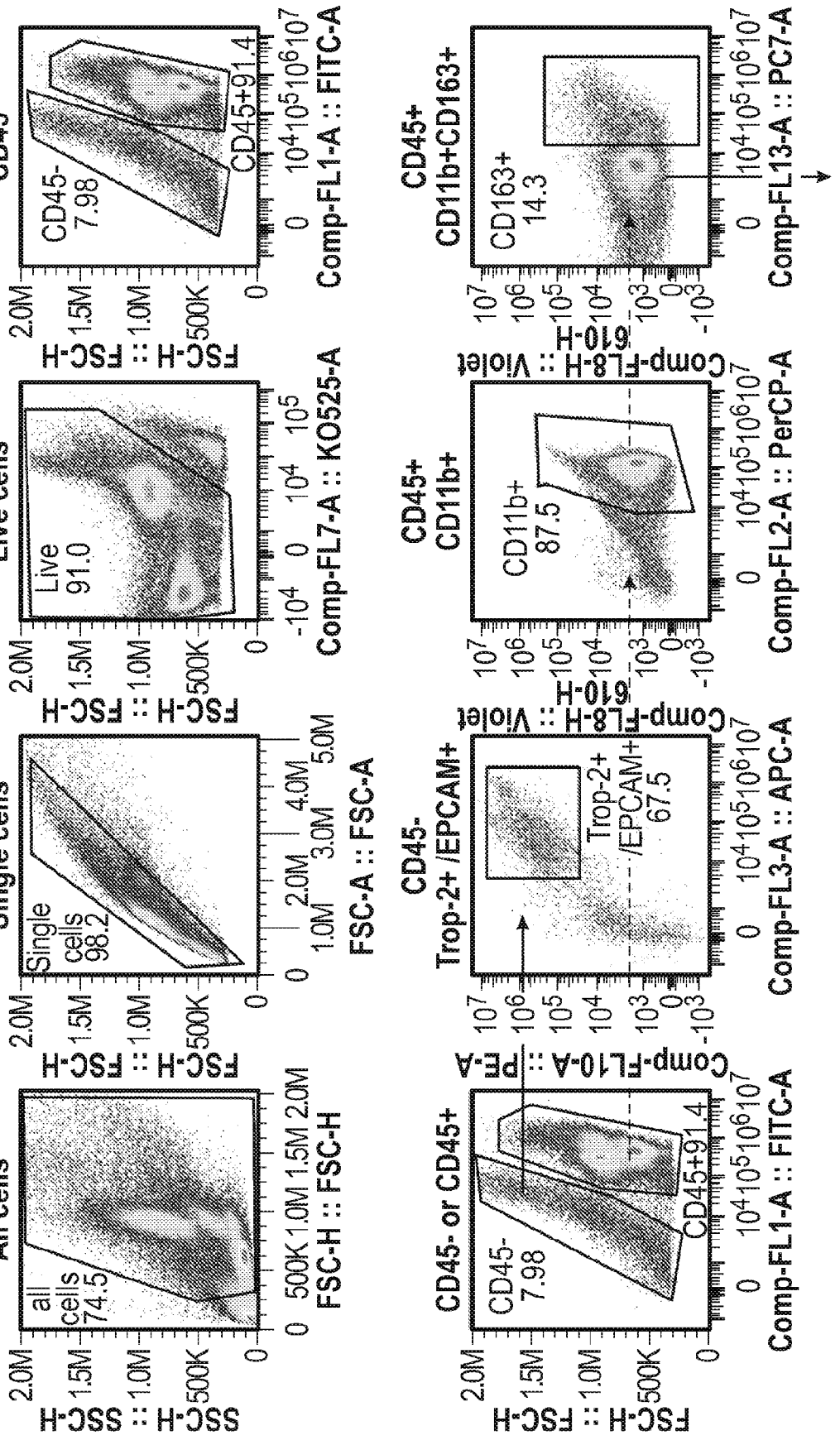

All cells
all cells 74.5
SSC-H :: FSC-H
FSC-H :: FSC-H
Single cells
Single cells 98.2
FSC-H :: FSC-H
FSC-A :: FSC-A
Live cells
Live 91.0
FSC-H :: FSC-H
Comp-FL7-A :: KO525-A
CD45
CD45- 7.98
CD45+91.4
FSC-H :: FSC-H
Comp-FL1-A :: FITC-A
CD45- or CD45+
CD45- 7.98
CD45+91.4
FSC-H :: FSC-H
Comp-FL1-A :: FITC-A
CD45- Trop-2+ /EPCAM+
Trop-2+ /EPCAM+ 67.5
Comp-FL10-A :: PE-A
Comp-FL3-A :: APC-A
CD45+ CD11b+
CD11b+ 87.5
Comp-FL8-H :: Violet
Comp-FL2-A :: PerCP-A
CD45+ CD11b+CD163+
CD163+ 14.3
610-H
Comp-FL13-A :: PC7-A

FIG. 57A

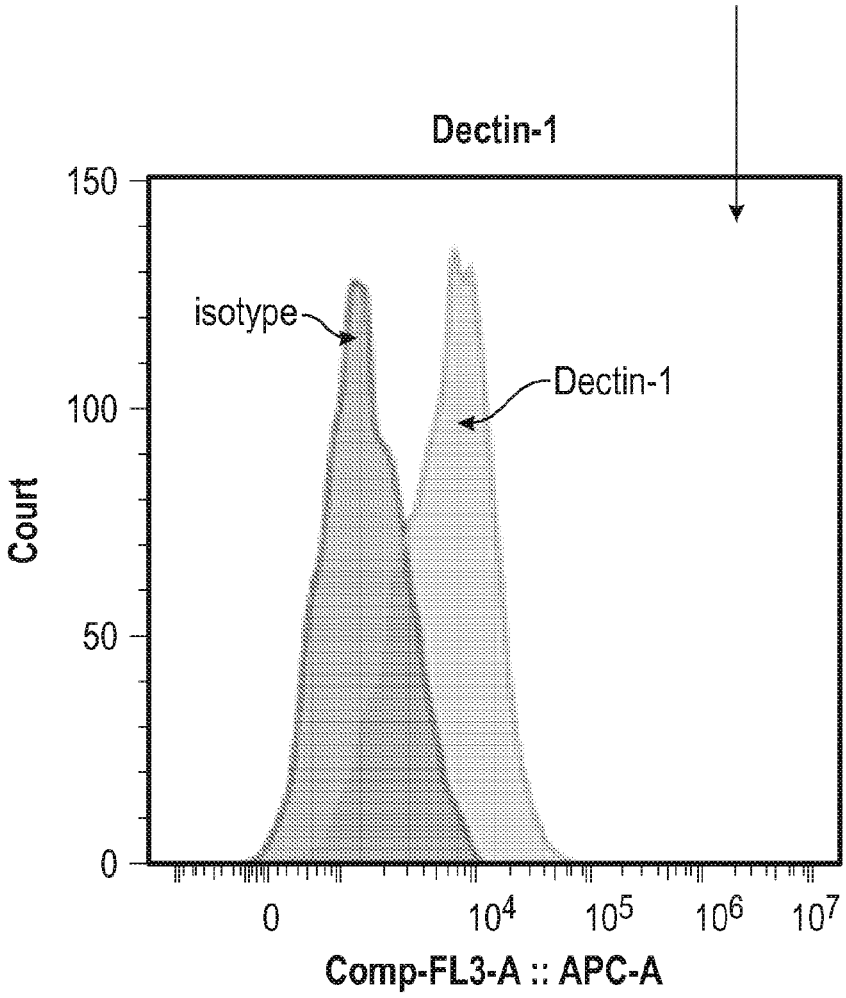

Dectin-1
150
100
50
0
Court
isotype
Dectin-1
0
10^4
10^5
10^6
10^7
Comp-FL3-A :: APC-A

FIG. 57B

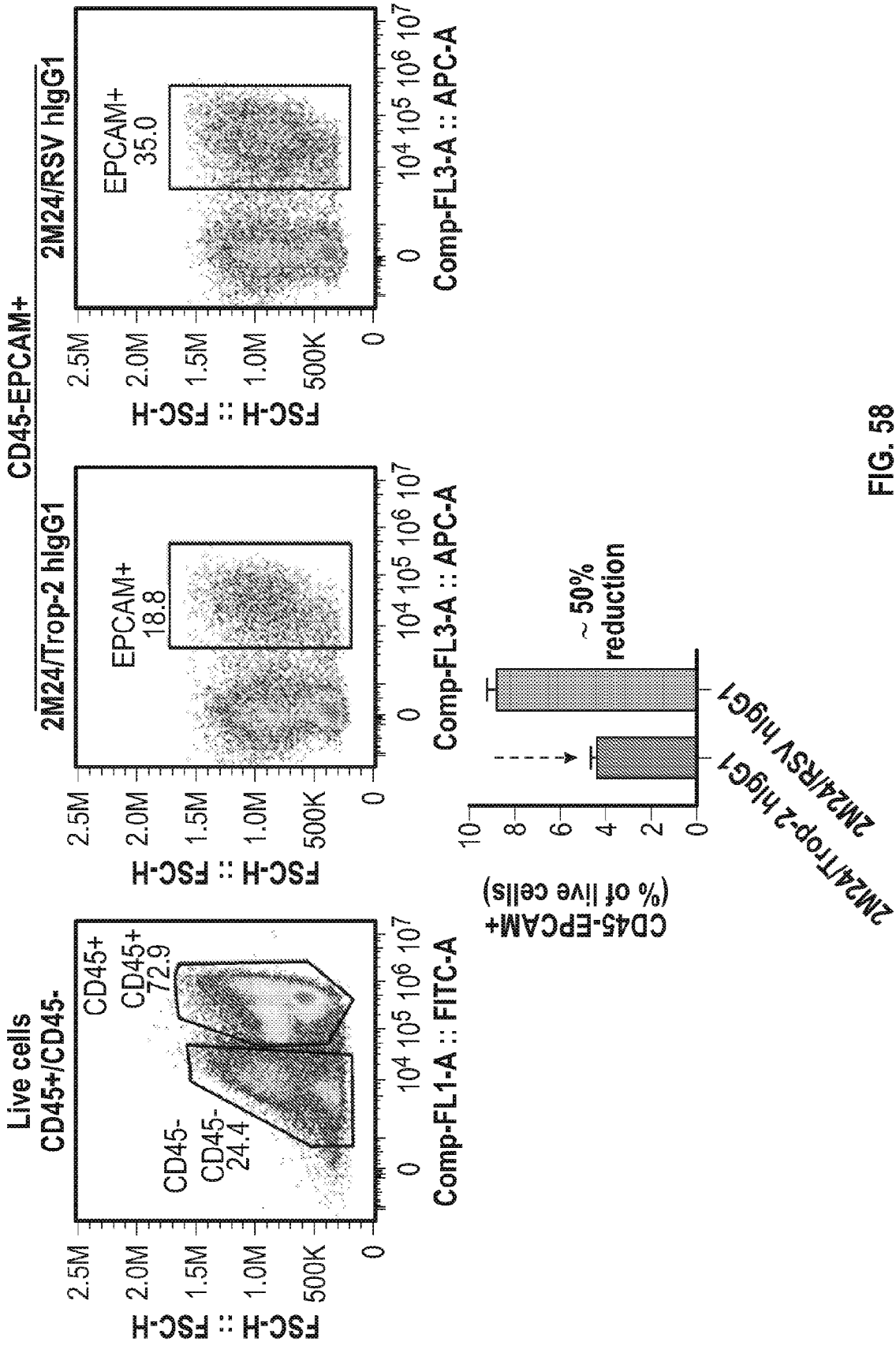

Live cells
CD45+/CD45-
CD45+
CD45+
72.9
CD45-
CD45-
24.4
FSC-H :: FSC-H
Comp-FL1-A :: FITC-A
2M24/Trop-2 hIgG1
EPCAM+
18.8
Comp-FL3-A :: APC-A
CD45-EPCAM+
2M24/RSV hIgG1
EPCAM+
35.0
Comp-FL3-A :: APC-A
~ 50%
reduction
CD45-EPCAM+
(% of live cells)
2M24/Trop-2 hIgG1
2M24/RSV hIgG1

FIG. 58

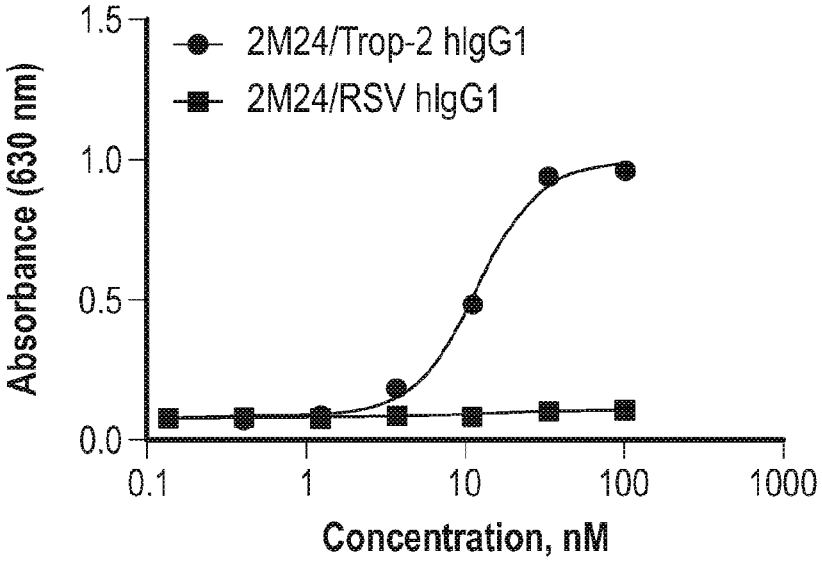

1.5
1.0
0.5
0.0
Absorbance (630 nm)
2M24/Trop-2 hIgG1
2M24/RSV hIgG1
0.1
1
10
100
1000
Concentration, nM

FIG. 59A

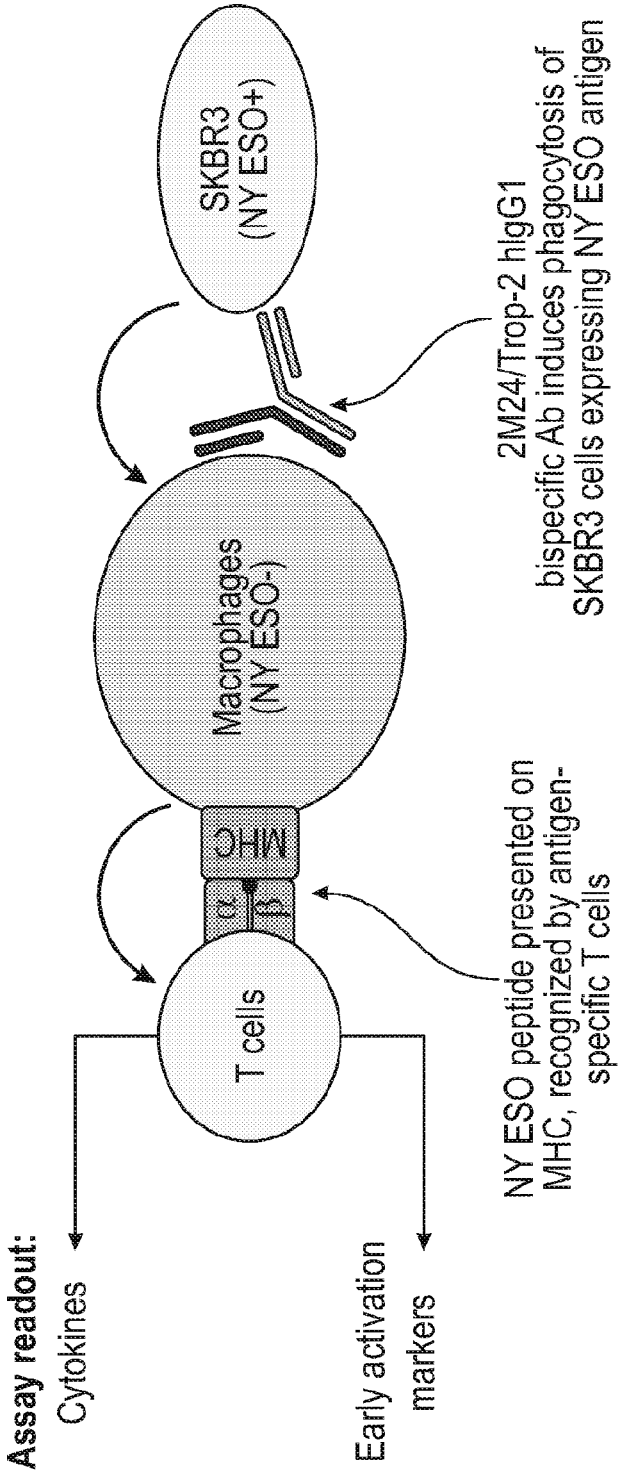

SKBR3
(NY ESO+)
2M24/Trop-2 hIgG1
bispecific Ab induces phagocytosis of
SKBR3 cells expressing NY ESO antigen
Macrophages
(NY ESO-)
MHC
α
β
T cells
NY ESO peptide presented on
MHC, recognized by antigen-
specific T cells
Assay readout:
Cytokines
Early activation
markers

FIG. 59B

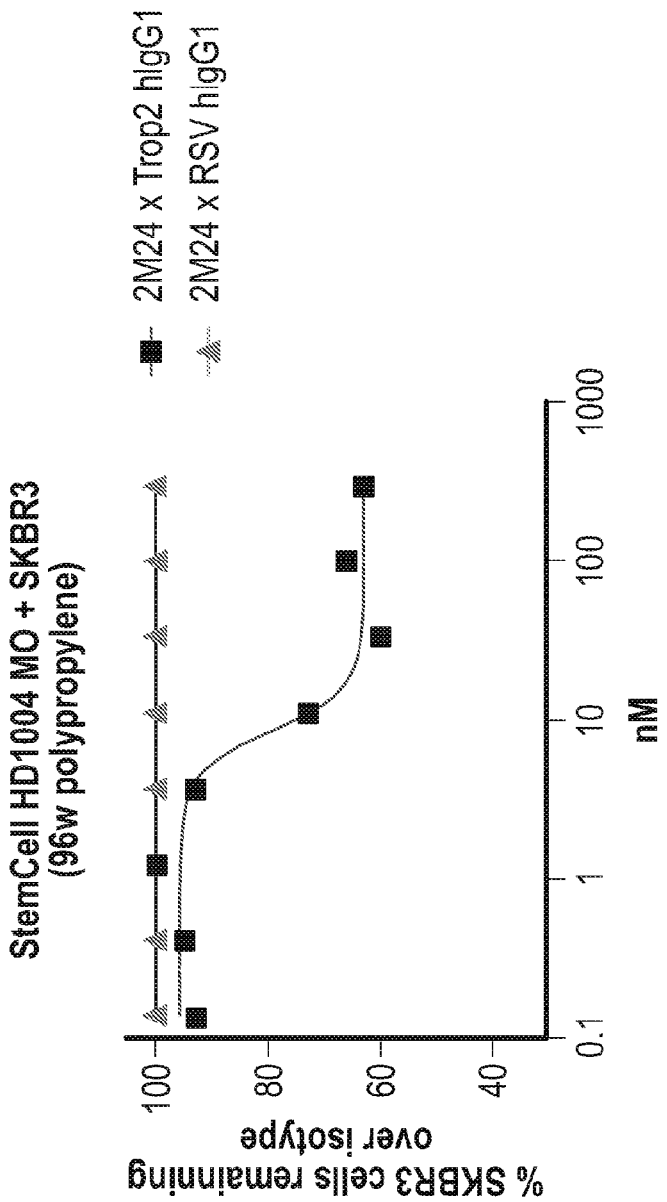

StemCell HD1004 MO + SKBR3
(96w polypropylene)
2M24 x Trop2 hIgG1
2M24 x RSV hIgG1
% SKBR3 cells remainning
over isotype
100
80
60
40
0.1
1
10
100
1000
nM

FIG. 59C

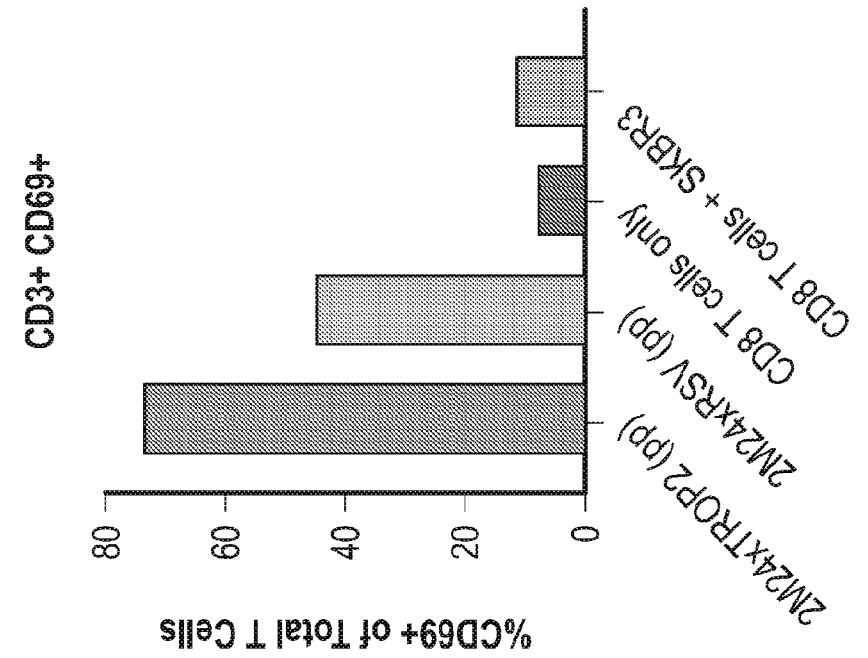


FIG. 59E

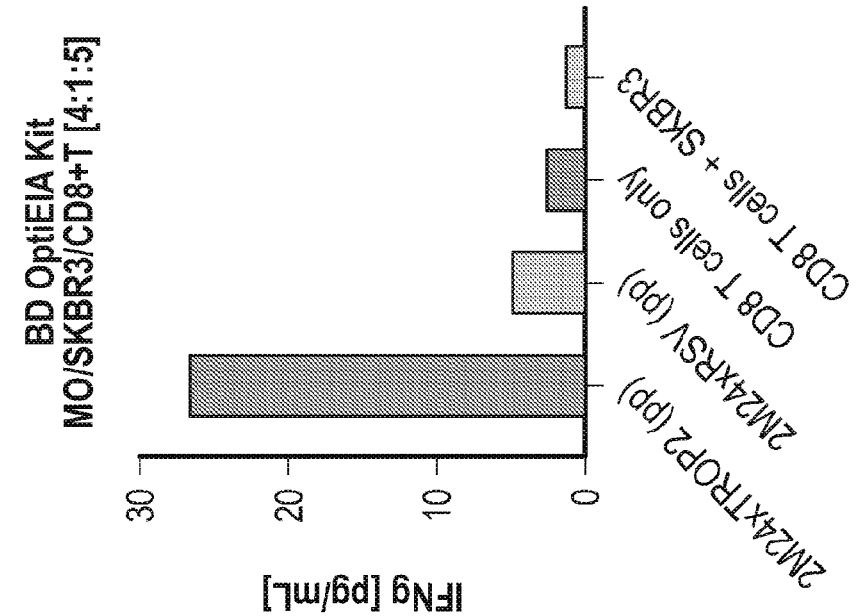


FIG. 59D

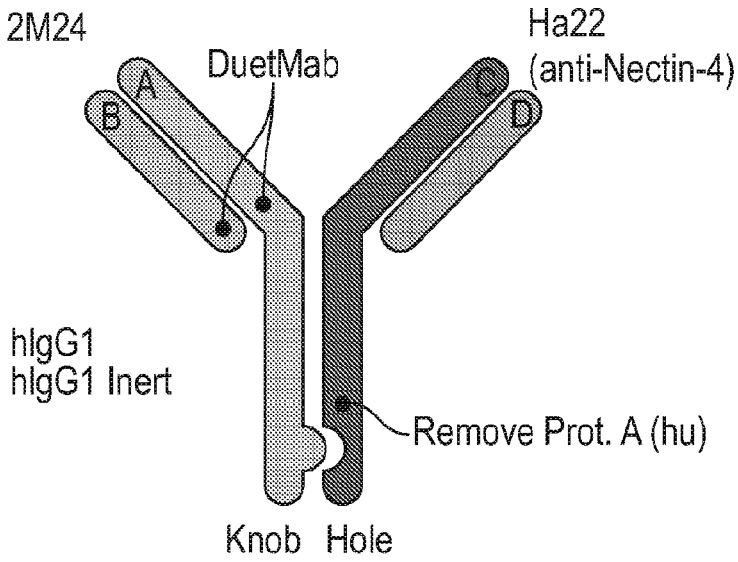

2M24
DuetMab
Ha22
(anti-Nectin-4)
A
B
C
D
hIgG1
hIgG1 Inert
Remove Prot. A (hu)
Knob
Hole

FIG. 60A

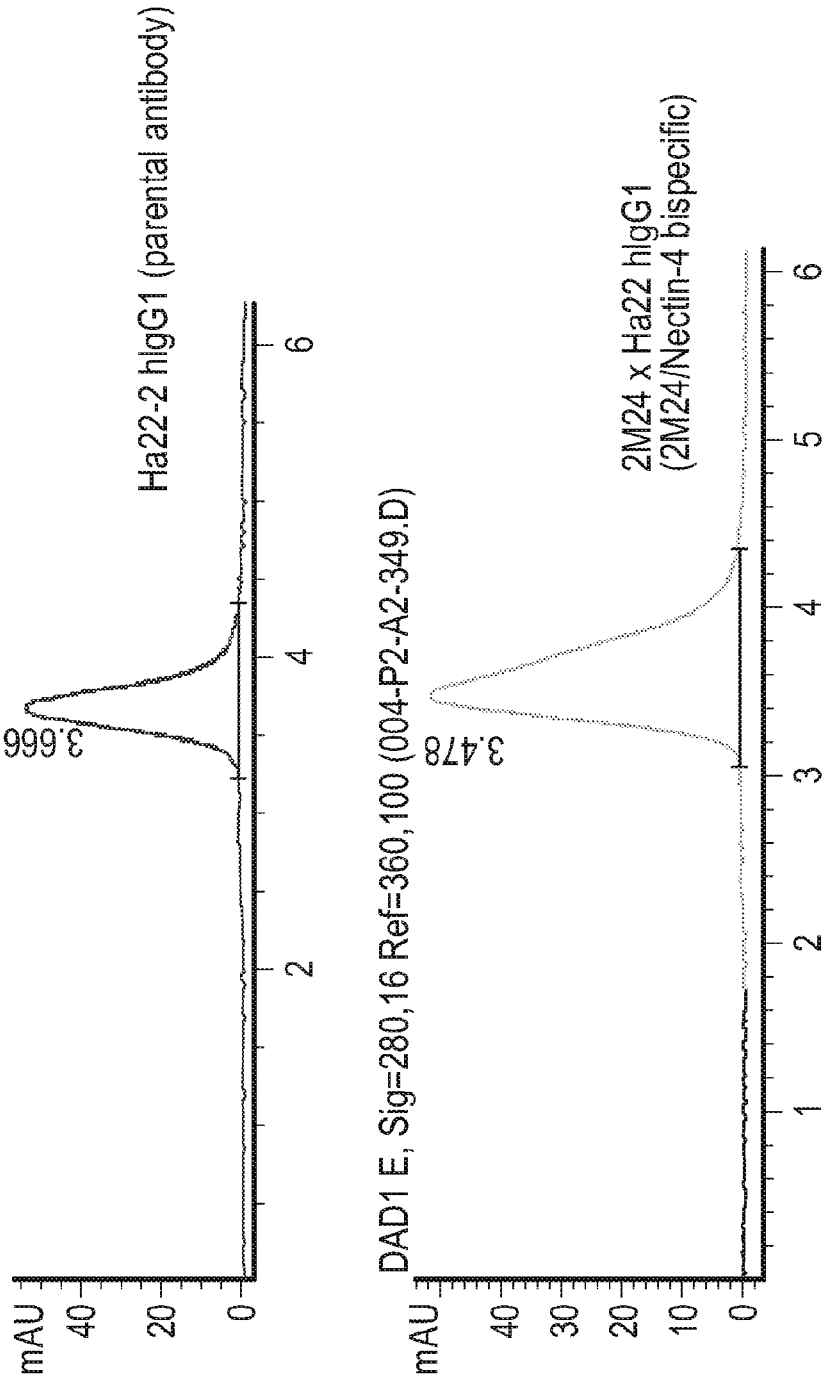

DAD1 E, Sig=280,16 Ref=360,100 (chanty\DEF_LC 2021-02-24 10-10-4
Ha22-2 hIgG1 (parental antibody)
3.666
mAU
40
20
0
2
4
6
DAD1 E, Sig=280,16 Ref=360,100 (004-P2-A2-349.D)
2M24 x Ha22 hIgG1
(2M24/Nectin-4 bispecific)
3.478
mAU
40
30
20
10
0
1
2
3
4
5
6

FIG. 60B

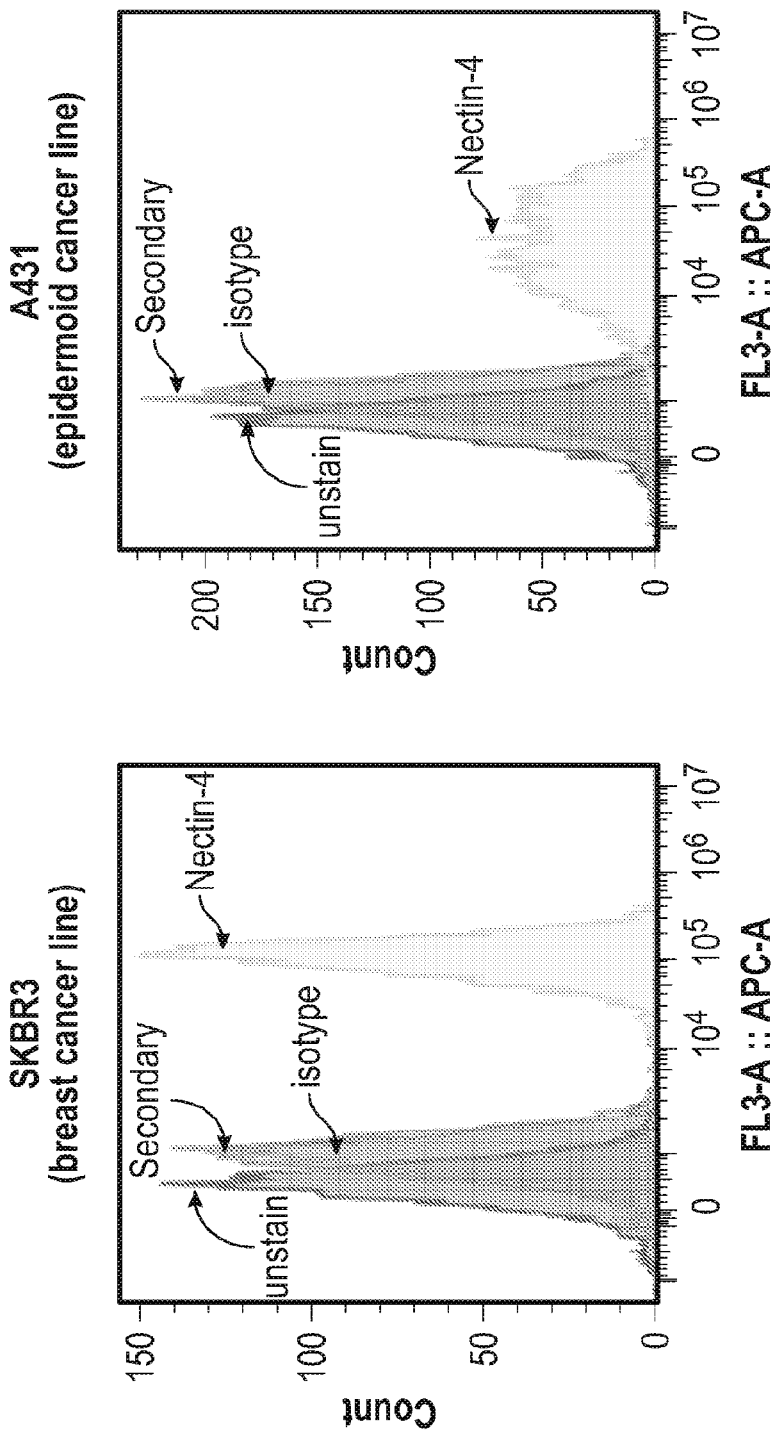

A431
(epidermoid cancer line)
Secondary
isotype
unstain
Nectin-4
Count
FL3-A :: APC-A
SKBR3
(breast cancer line)
Secondary
isotype
unstain
Nectin-4
Count
FL3-A :: APC-A

FIG. 61A

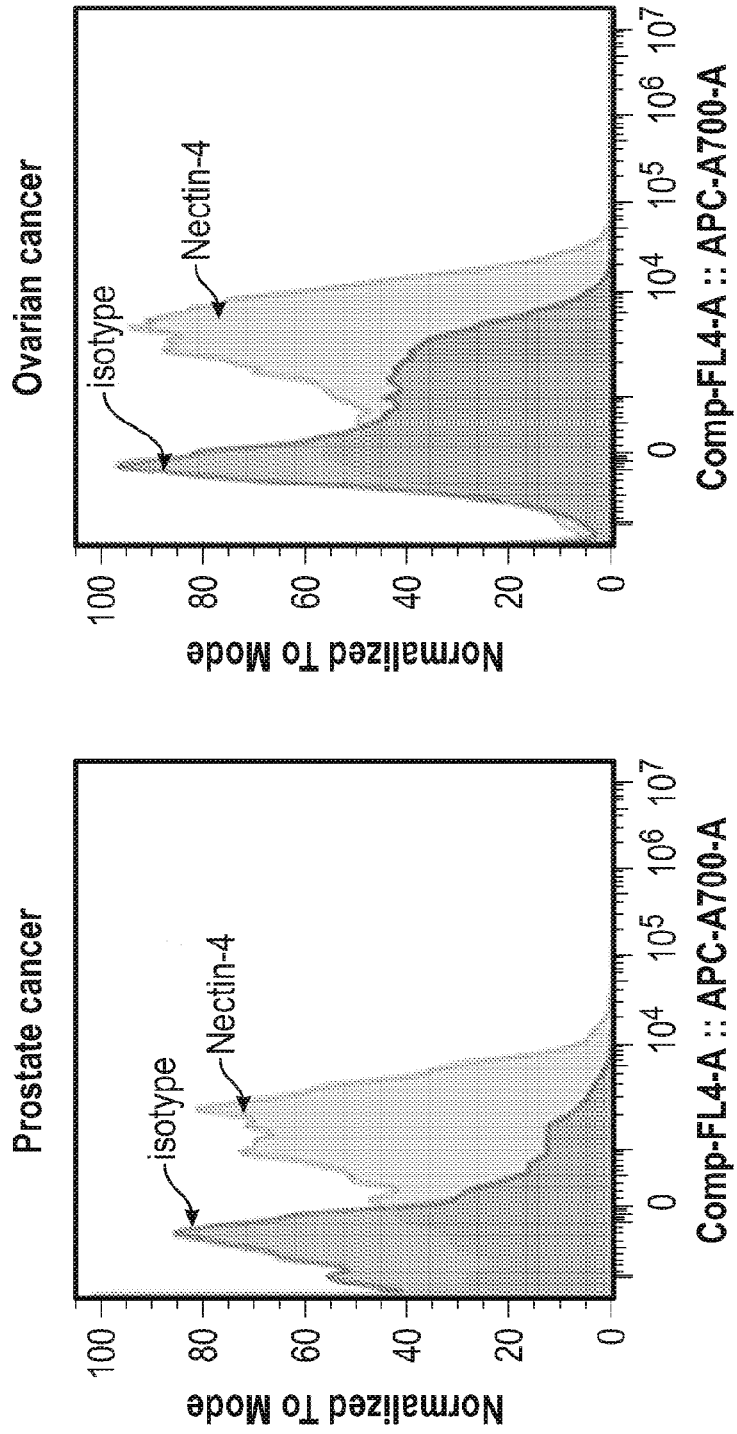

Ovarian cancer
isotype
Nectin-4
Normalized To Mode
100
80
60
40
20
0
0
10^4
10^5
10^6
10^7
Comp-FL4-A :: APC-A700-A
Prostate cancer
isotype
Nectin-4
Normalized To Mode
100
80
60
40
20
0
0
10^4
10^5
10^6
10^7
Comp-FL4-A :: APC-A700-A

FIG. 61B

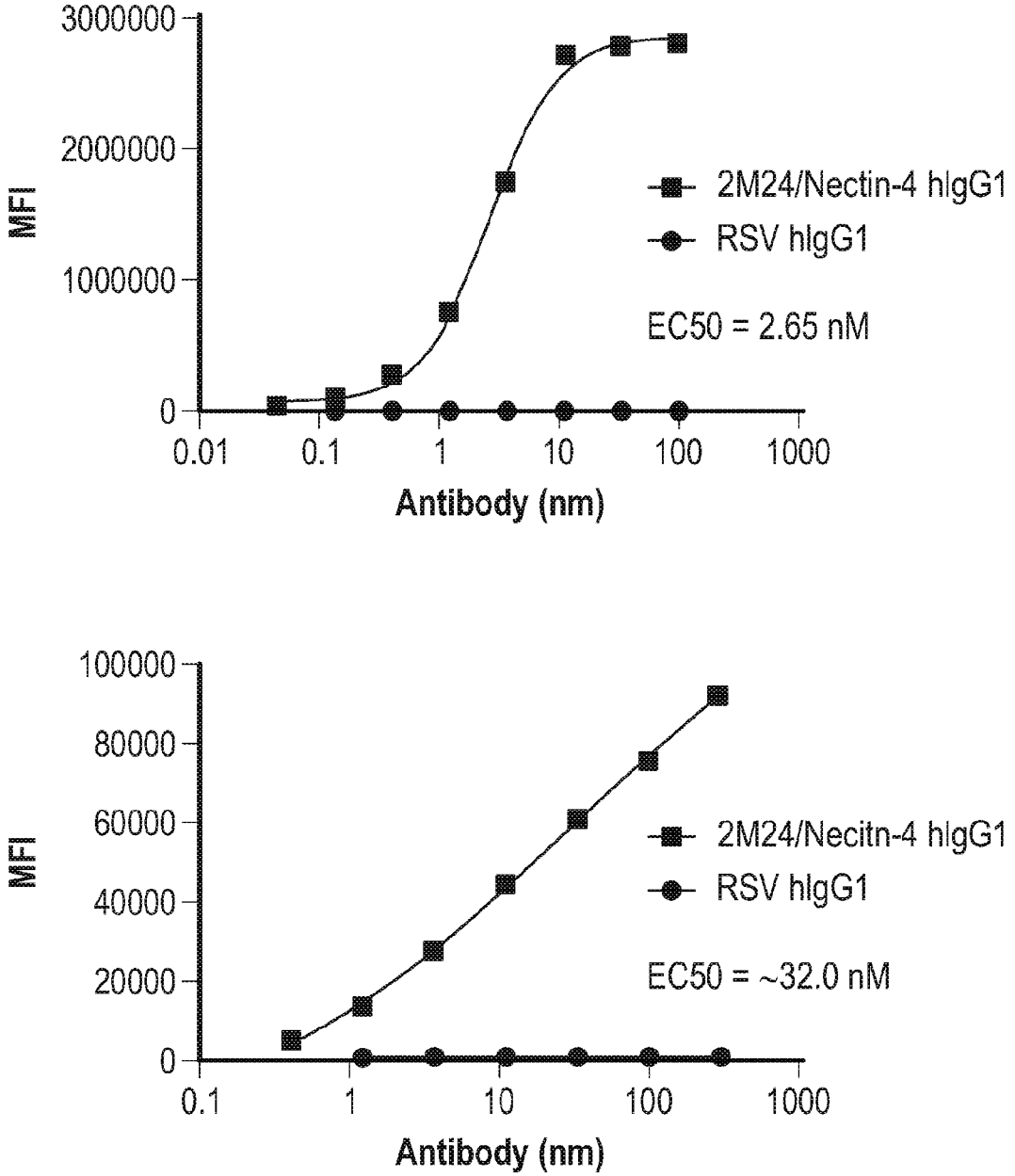

3000000
2000000
1000000
0
MFI
0.01
0.1
1
10
100
1000
Antibody (nm)
2M24/Nectin-4 hIgG1
RSV hIgG1
EC50 = 2.65 nM
100000
80000
60000
40000
20000
0
MFI
0.1
1
10
100
1000
Antibody (nm)
2M24/Necitn-4 hIgG1
RSV hIgG1
EC50 = ~32.0 nM

FIG. 62

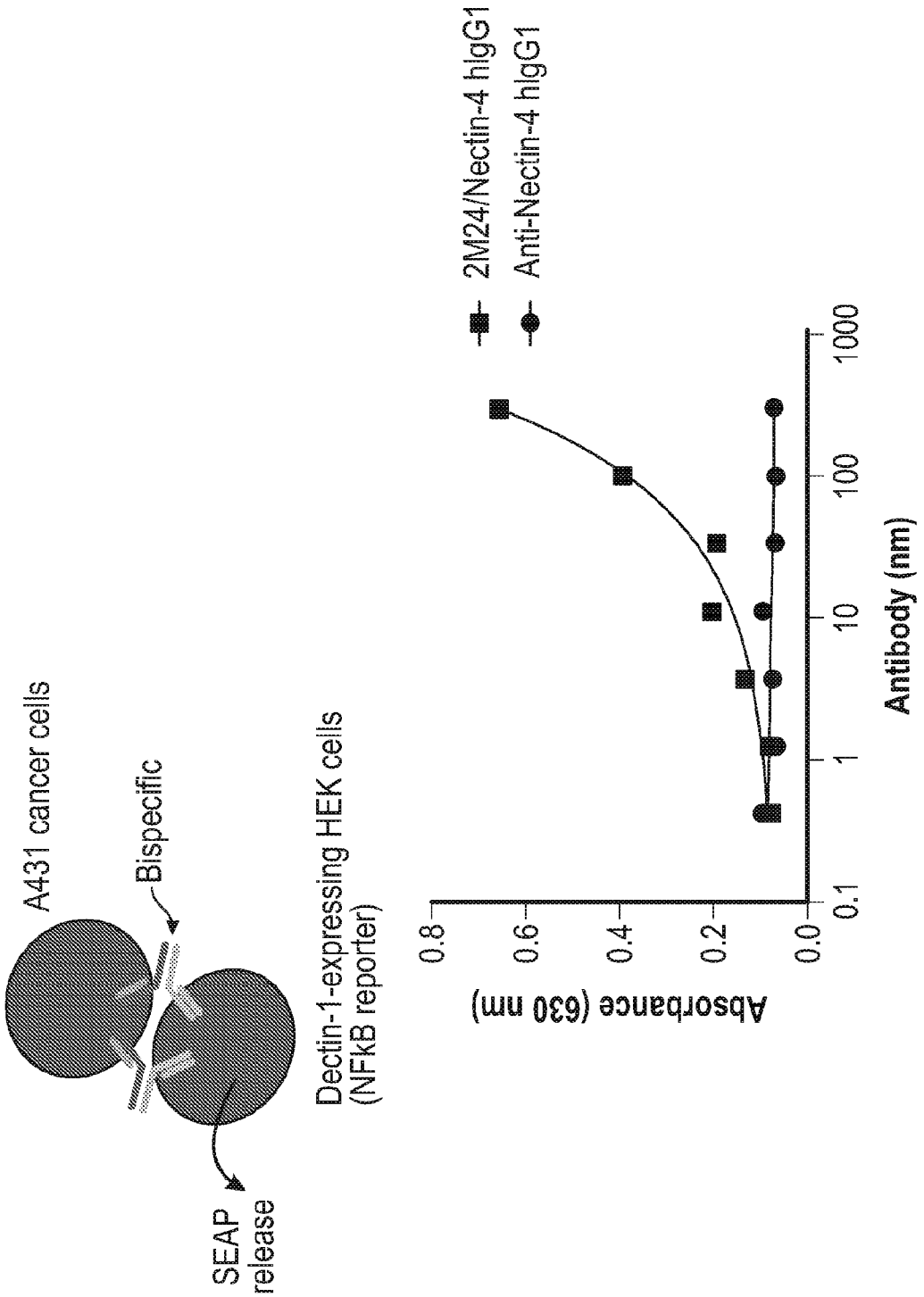

A431 cancer cells
Bispecific
Dectin-1-expressing HEK cells
(NFkB reporter)
SEAP
release
2M24/Nectin-4 hIgG1
Anti-Nectin-4 hIgG1
Absorbance (630 nm)
0.0
0.2
0.4
0.6
0.8
0.1
1
10
100
1000
Antibody (nm)

FIG. 63

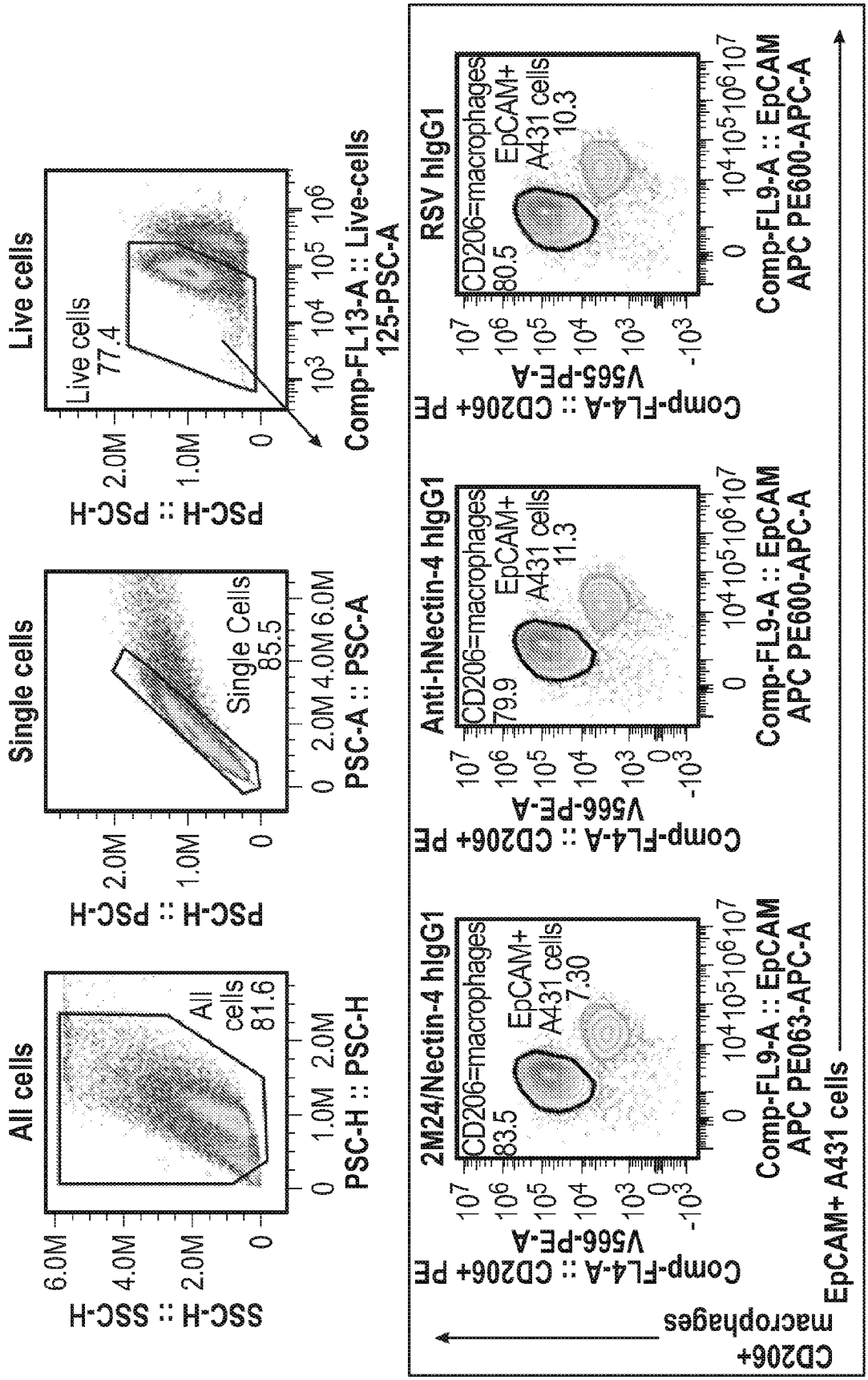

All cells
All cells 81.6
SSC-H :: SSC-H
PSC-H :: PSC-H
Single cells
Single Cells 85.5
PSC-H :: PSC-H
PSC-A :: PSC-A
Live cells
Live cells 77.4
PSC-H :: PSC-H
Comp-FL13-A :: Live-cells 125-PSC-A
EpCAM+ A431 cells
CD206+ macrophages
2M24/Nectin-4 hIgG1
CD206=macrophages 83.5
EpCAM+ A431 cells 7.30
Comp-FL4-A :: CD206+ PE V566-PE-A
Comp-FL9-A :: EpCAM APC PE063-APC-A
Anti-hNectin-4 hIgG1
CD206=macrophages 79.9
EpCAM+ A431 cells 11.3
Comp-FL4-A :: CD206+ PE V566-PE-A
Comp-FL9-A :: EpCAM APC PE600-APC-A
RSV hIgG1
CD206=macrophages 80.5
EpCAM+ A431 cells 10.3
Comp-FL4-A :: CD206+ PE V565-PE-A
Comp-FL9-A :: EpCAM APC PE600-APC-A

FIG. 64A

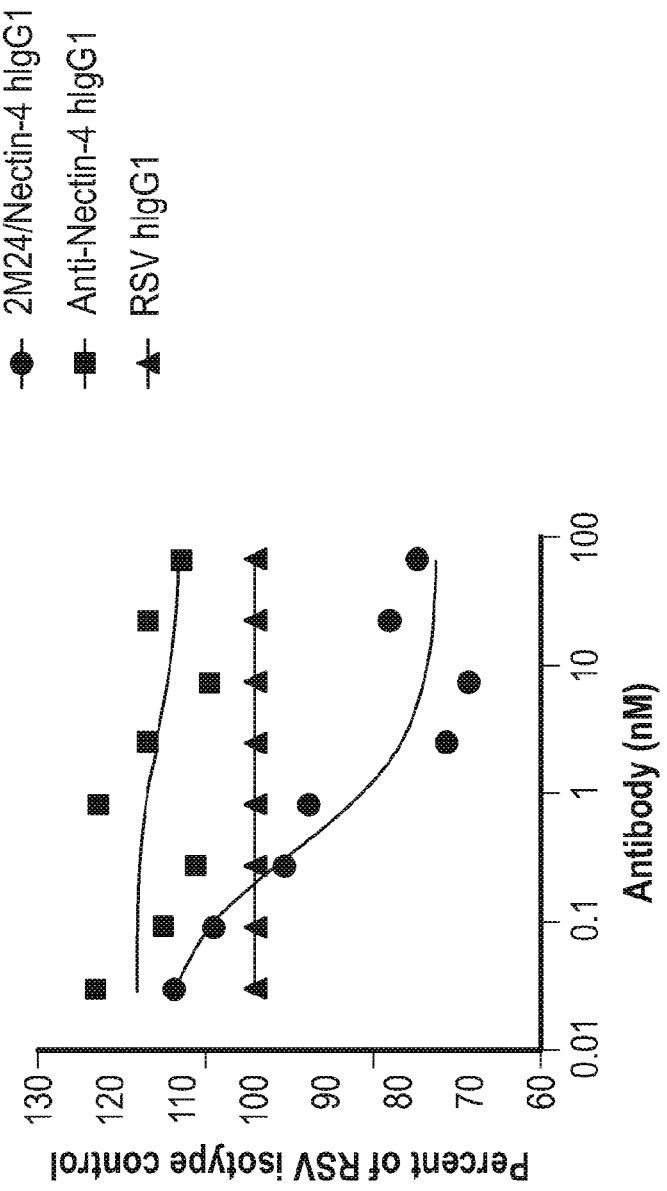

2M24/Nectin-4 hIgG1
Anti-Nectin-4 hIgG1
RSV hIgG1
Percent of RSV isotype control
130
120
110
100
90
80
70
60
0.01
0.1
1
10
100
Antibody (nM)

FIG. 64B

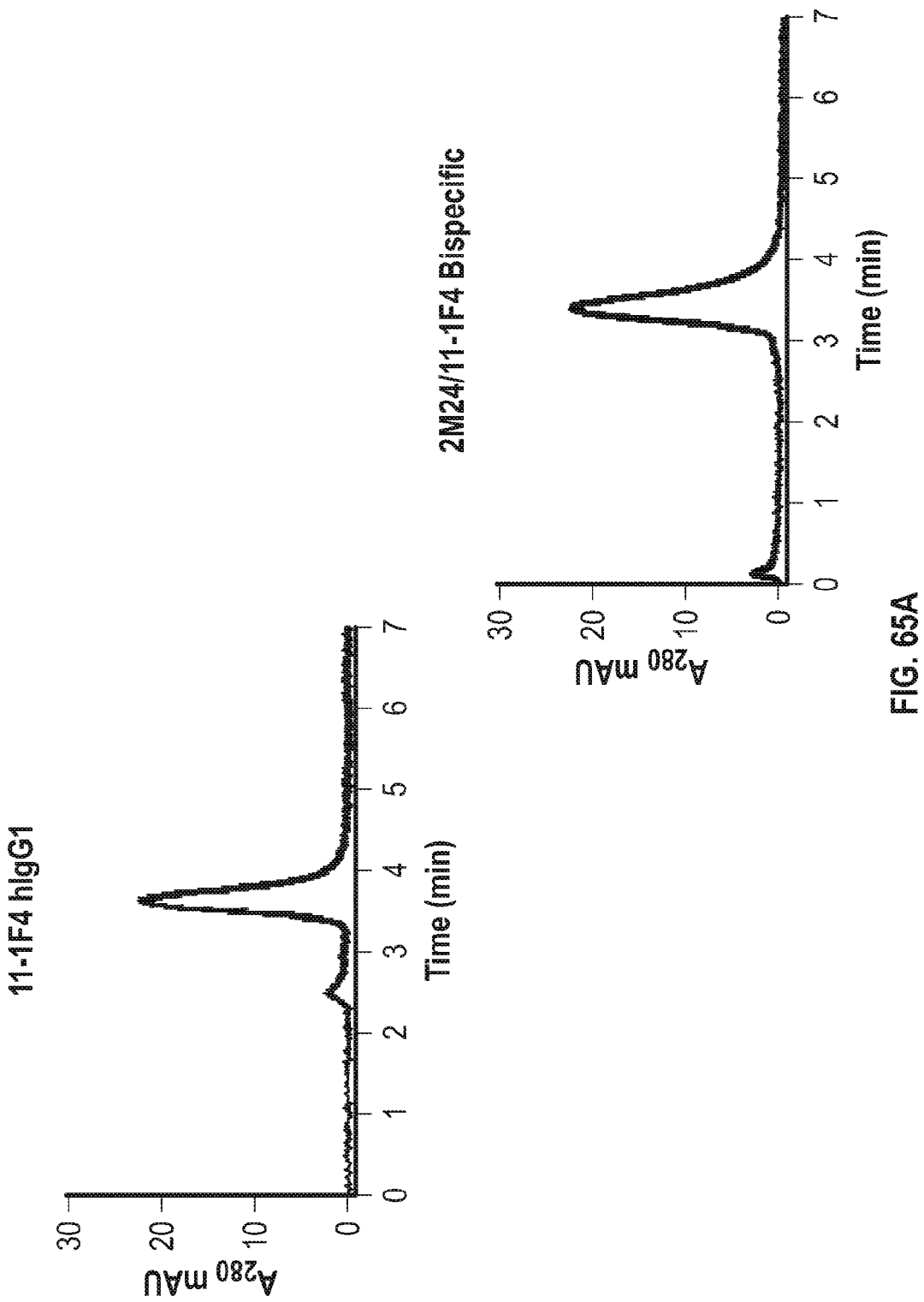

11-1F4 hIgG1
A_{280} mAU
30
20
10
0
0
1
2
3
4
5
6
7
Time (min)
2M24/11-1F4 Bispecific
A_{280} mAU
30
20
10
0
0
1
2
3
4
5
6
7
Time (min)

FIG. 65A

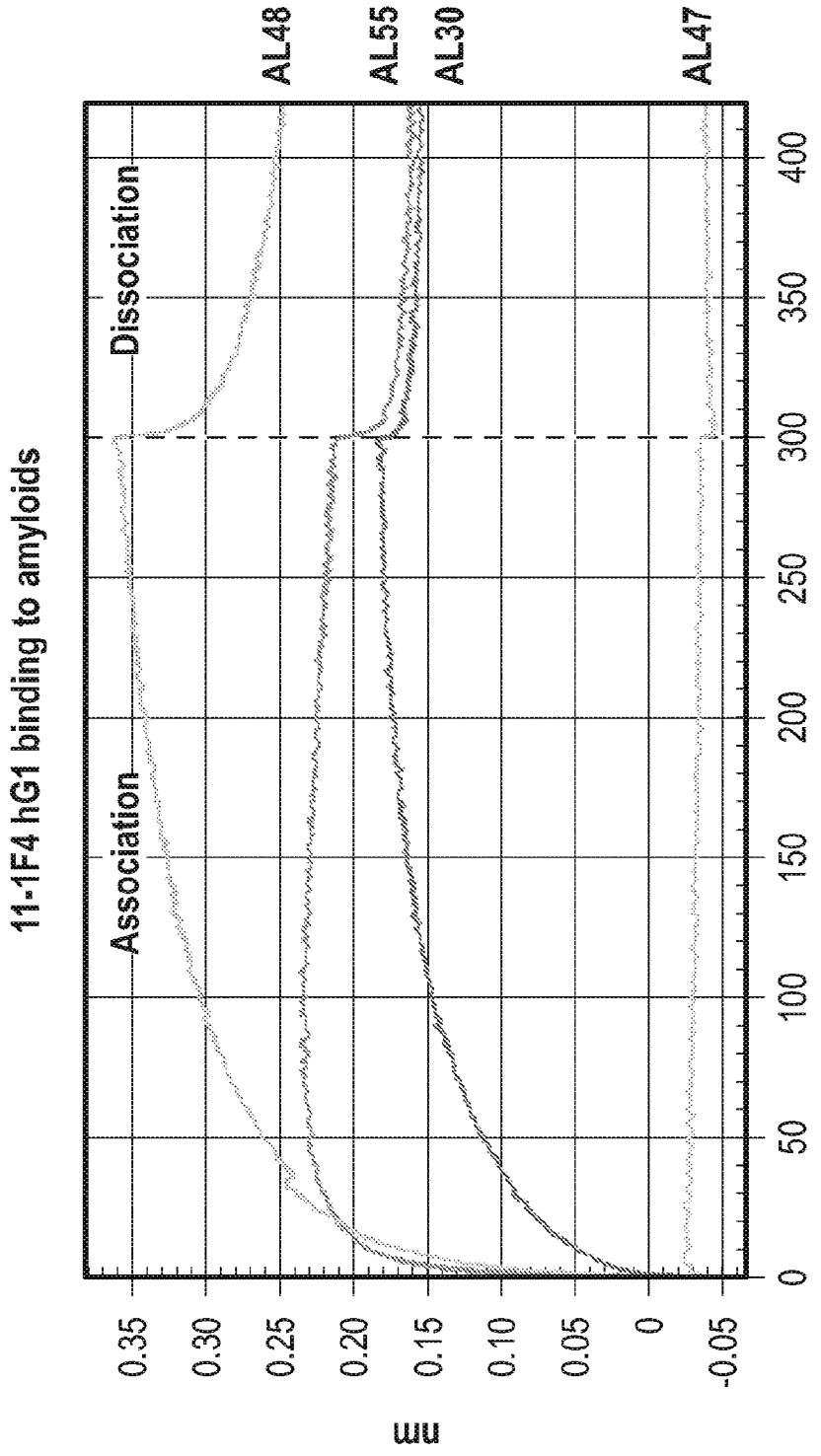

11-1F4 hG1 binding to amyloids
Association
Dissociation
AL48
AL55
AL30
AL47
nm
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
-0.05
0
50
100
150
200
250
300
350
400
Time (s)

FIG. 65B

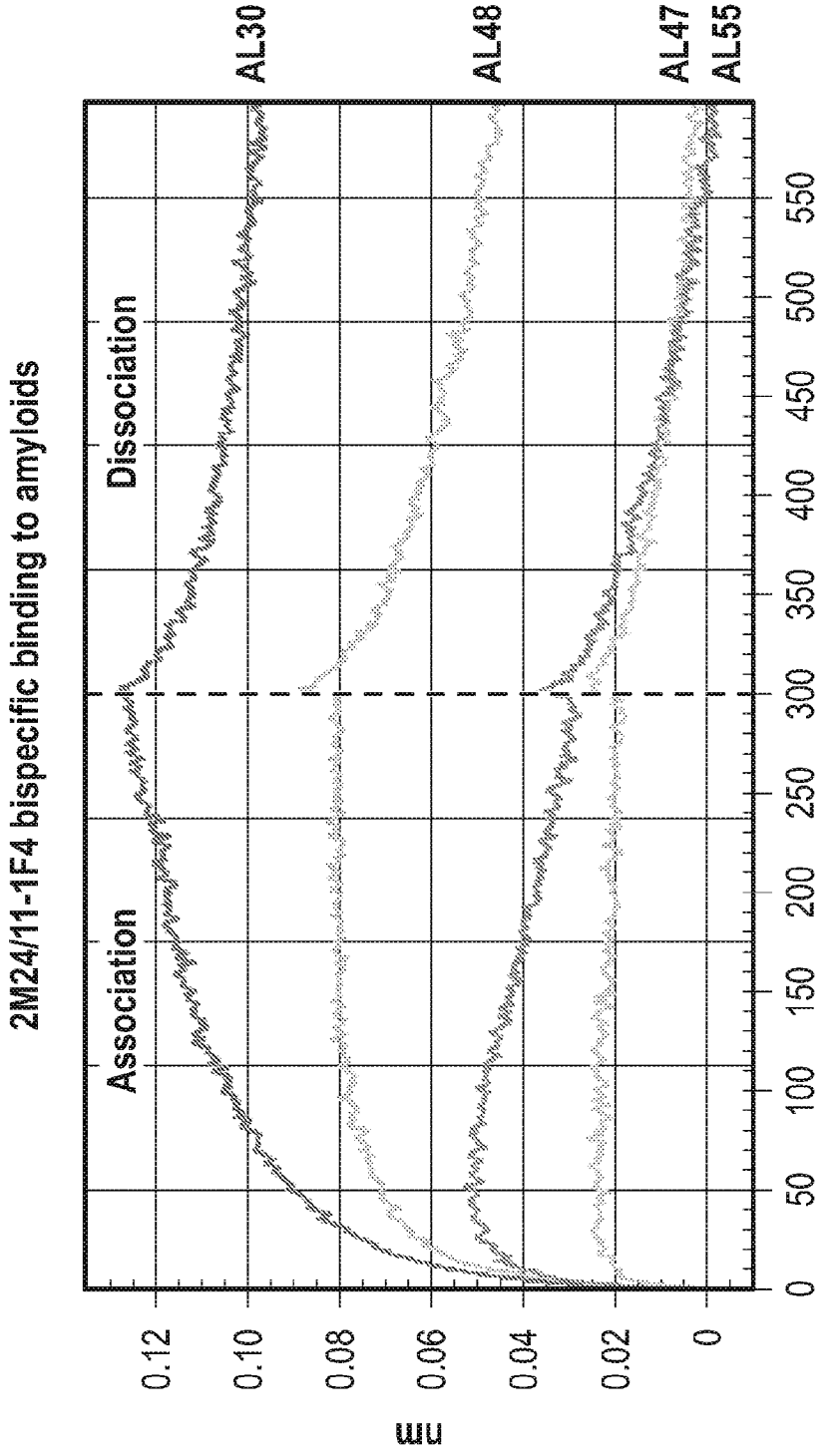

2M24/11-1F4 bispecific binding to amyloids
Association
Dissociation
AL30
AL48
AL47
AL55
nm
0.12
0.10
0.08
0.06
0.04
0.02
0
0
50
100
150
200
250
300
350
400
450
500
550
Time (s)

FIG. 65C

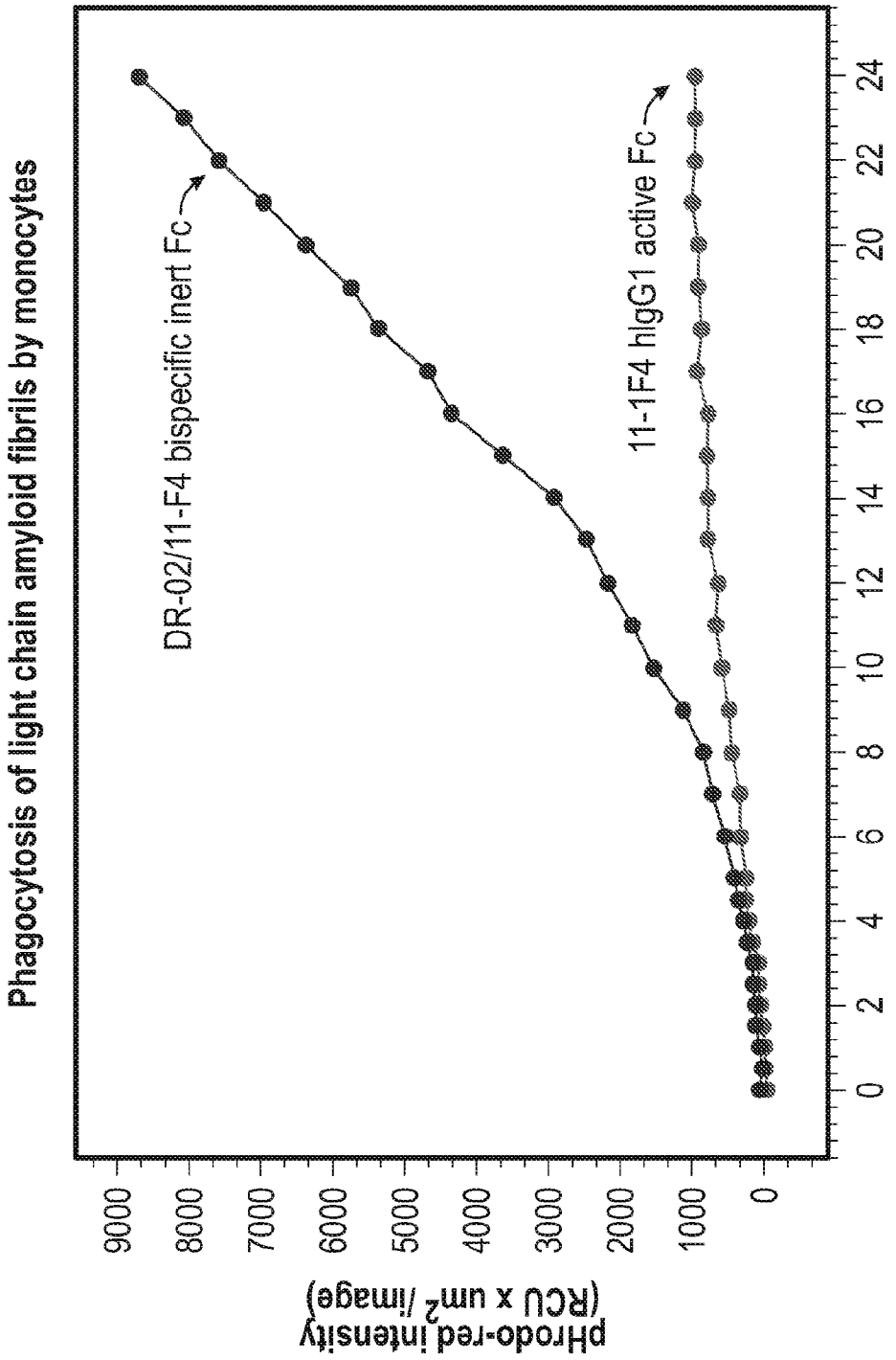

Phagocytosis of light chain amyloid fibrils by monocytes
pHrodo-red intensity (RCU x um2 /image)
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
0
2
4
6
8
10
12
14
16
18
20
22
24
Time (hour)
DR-02/11-F4 bispecific inert Fc
11-1F4 hIgG1 active Fc

FIG. 66

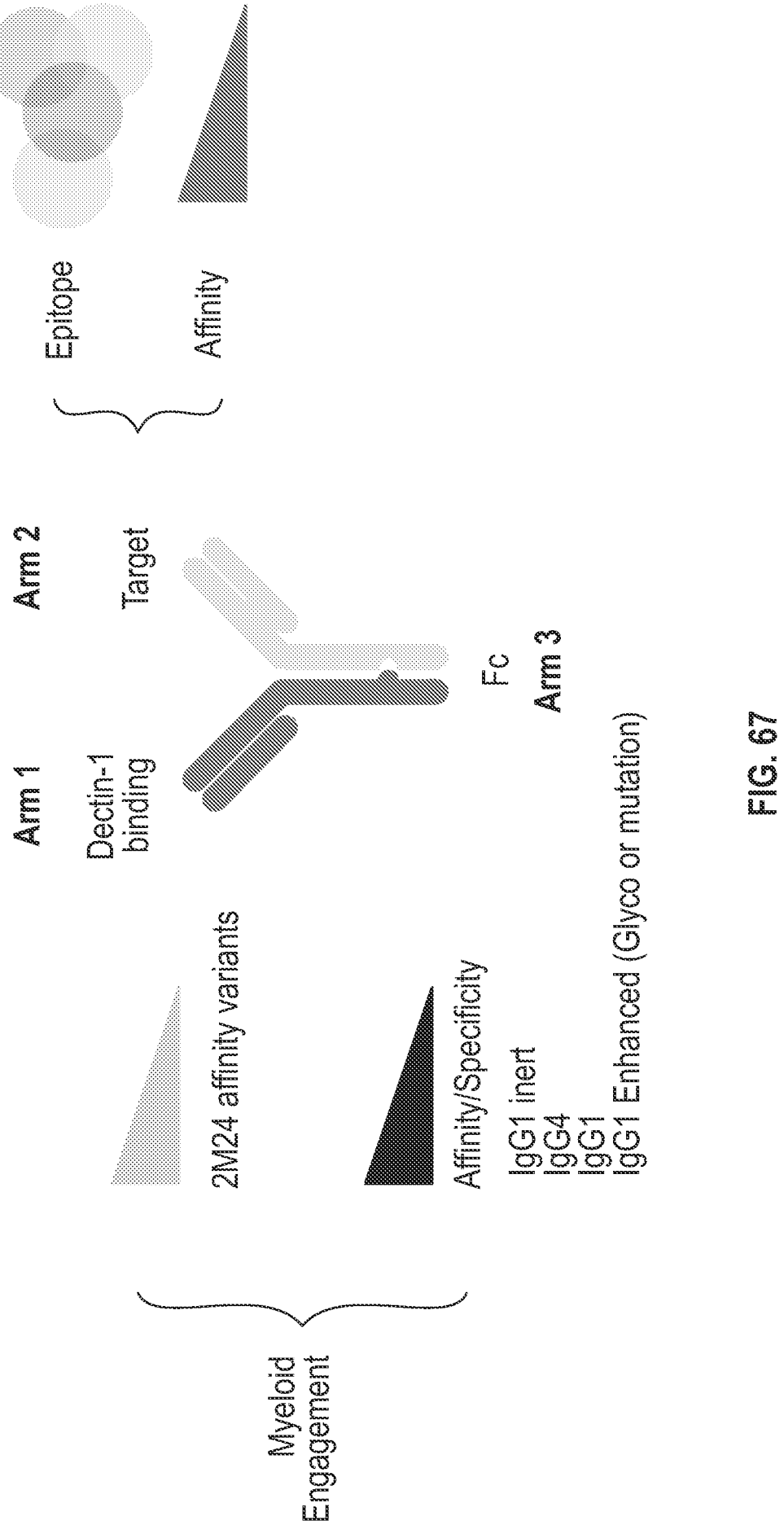

Epitope
Affinity
Arm 2
Target
Arm 1
Dectin-1 binding
Fc
Arm 3
2M24 affinity variants
Affinity/Specificity
IgG1 inert
IgG4
IgG1
IgG1 Enhanced (Glyco or mutation)
Myeloid Engagement

FIG. 67

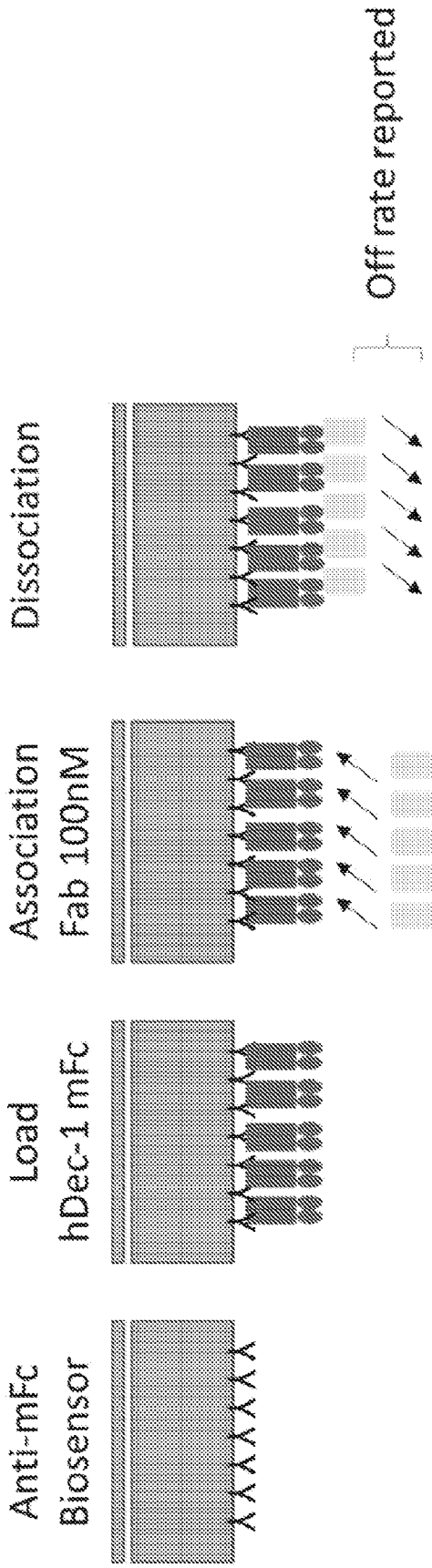

Anti-mFc Biosensor
Load hDec-1 mFc
Association Fab 100nM
Dissociation
Off rate reported
Fab

FIG. 68A

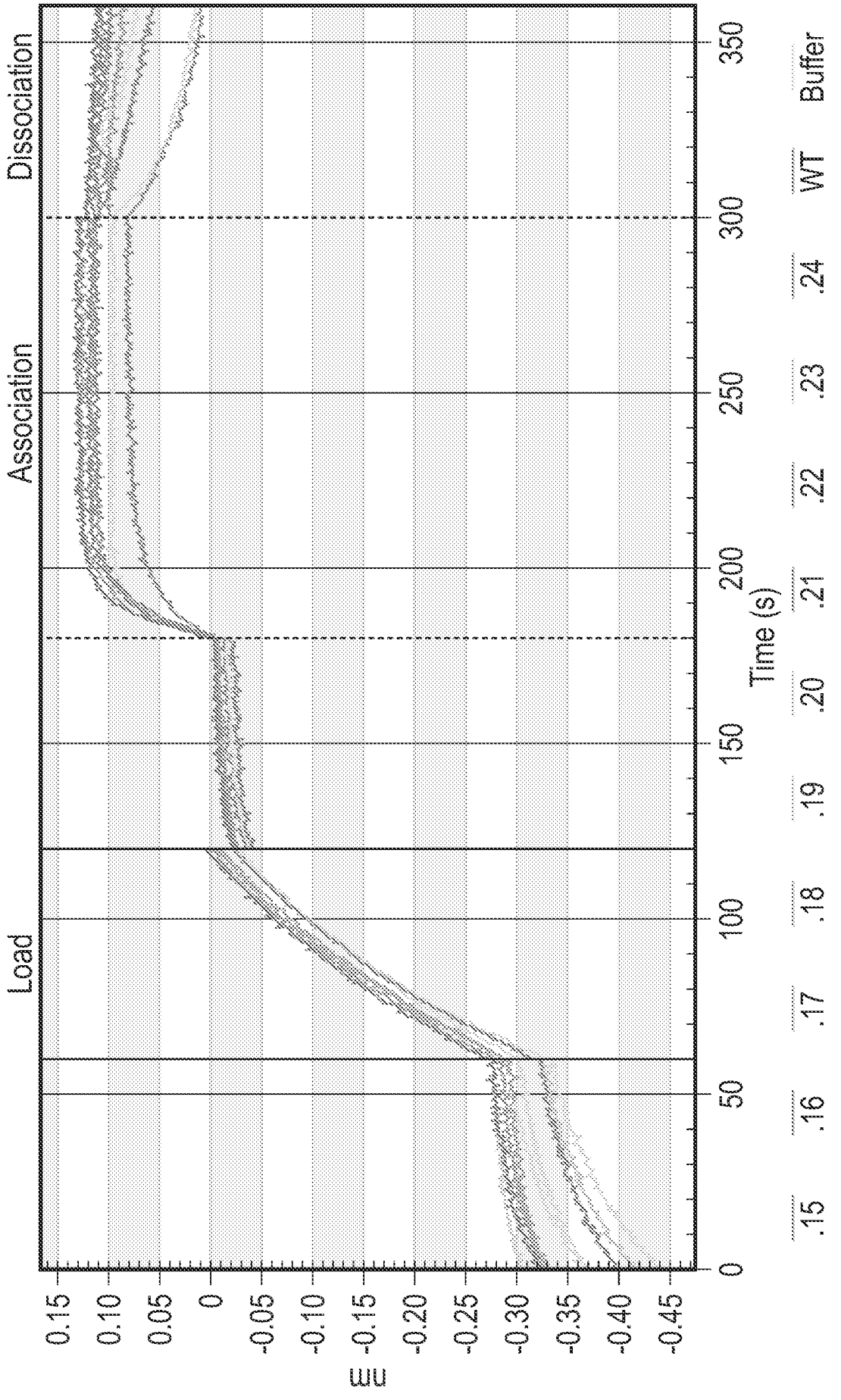

Load
Association
Dissociation
nm
0.15
0.10
0.05
0
-0.05
-0.10
-0.15
-0.20
-0.25
-0.30
-0.35
-0.40
-0.45
0
50
100
150
200
250
300
350
Time (s)
.15
.16
.17
.18
.19
.20
.21
.22
.23
.24
WT
Buffer

FIG. 68B

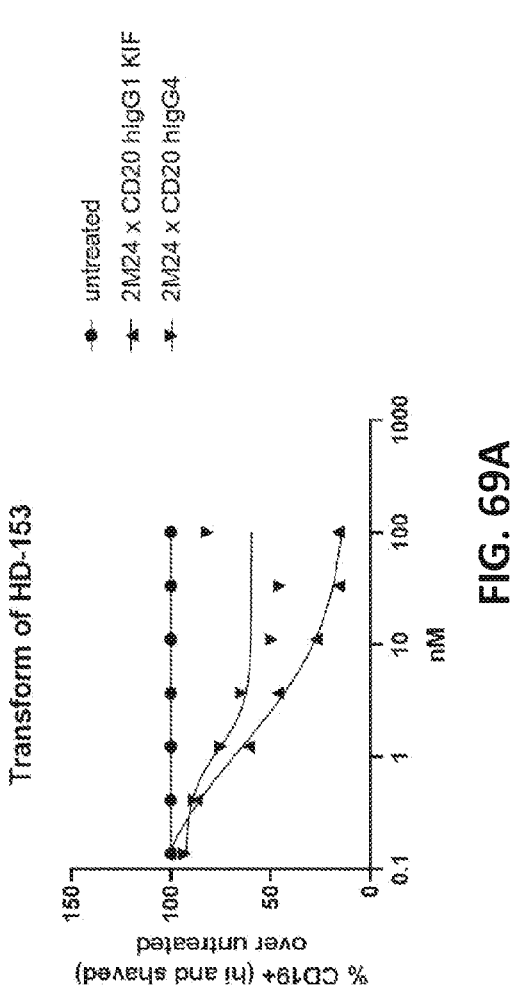


FIG. 69A

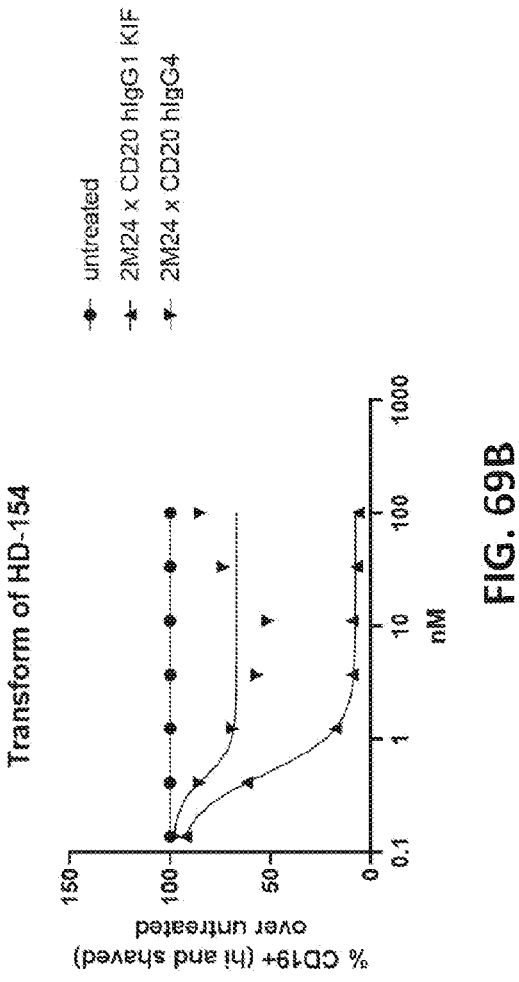


FIG. 69B

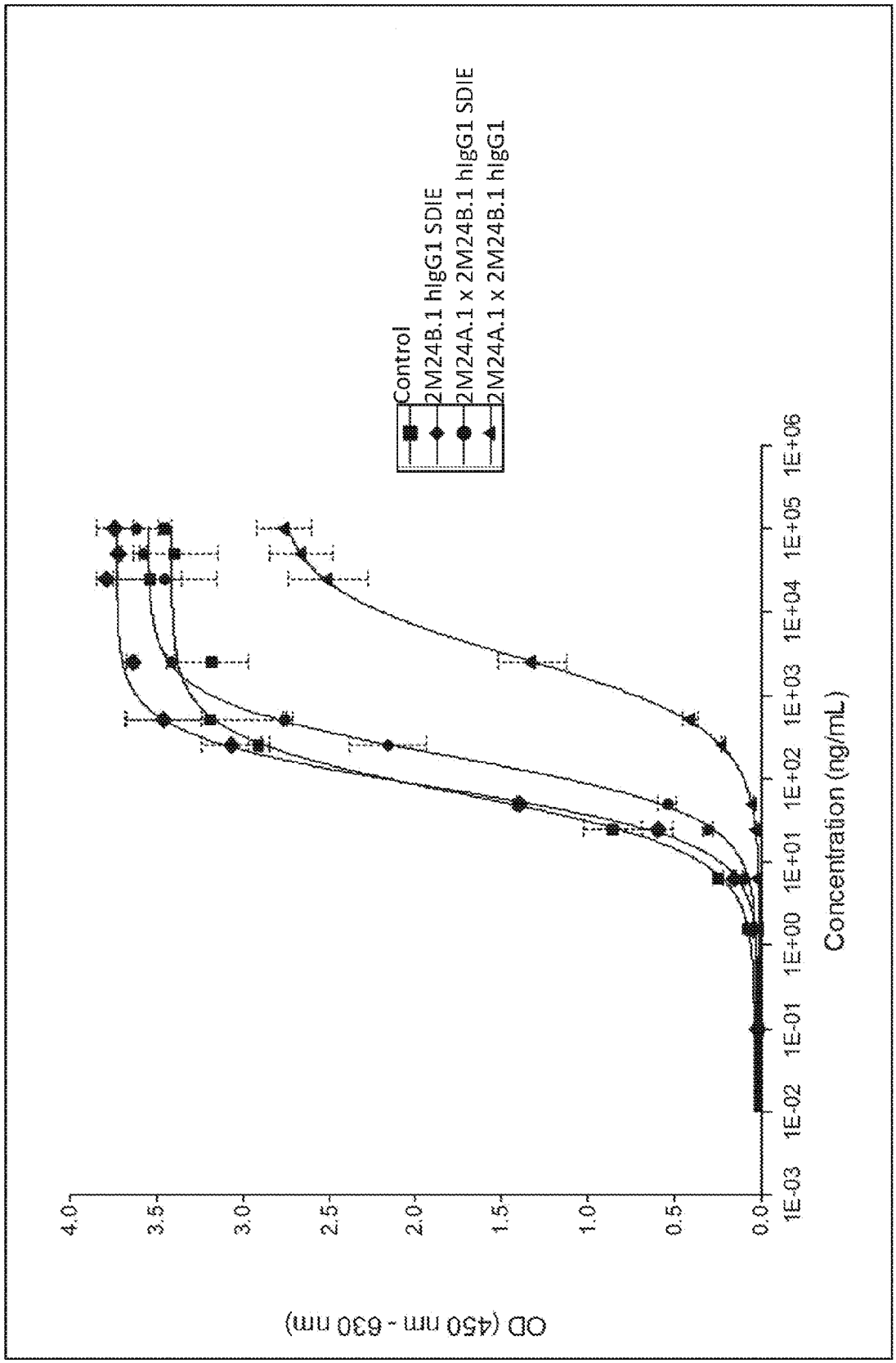

OD (450 nm - 630 nm)
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
1E-03
1E-02
1E-01
1E+00
1E+01
1E+02
1E+03
1E+04
1E+05
1E+06
Concentration (ng/mL)
Control
2M24B.1 hIgG1 SDIE
2M24A.1 x 2M24B.1 hIgG1 SDIE
2M24A.1 x 2M24B.1 hIgG1

FIG. 70A

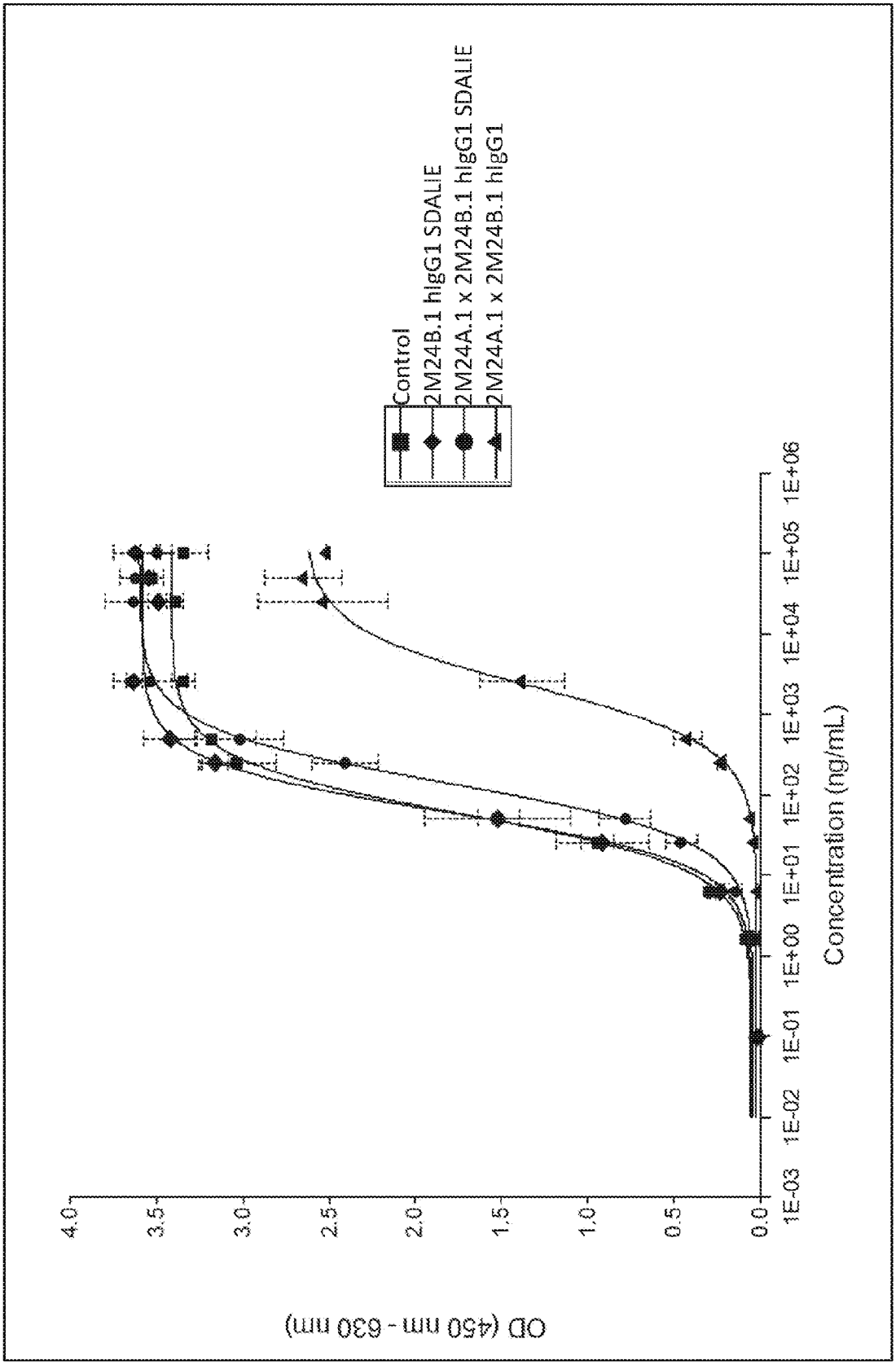

Control
2M24B.1 hIgG1 SDALIE
2M24A.1 x 2M24B.1 hIgG1 SDALIE
2M24A.1 x 2M24B.1 hIgG1
OD (450 nm - 630 nm)
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
1E-03
1E-02
1E-01
1E+00
1E+01
1E+02
1E+03
1E+04
1E+05
1E+06
Concentration (ng/mL)

FIG. 70B

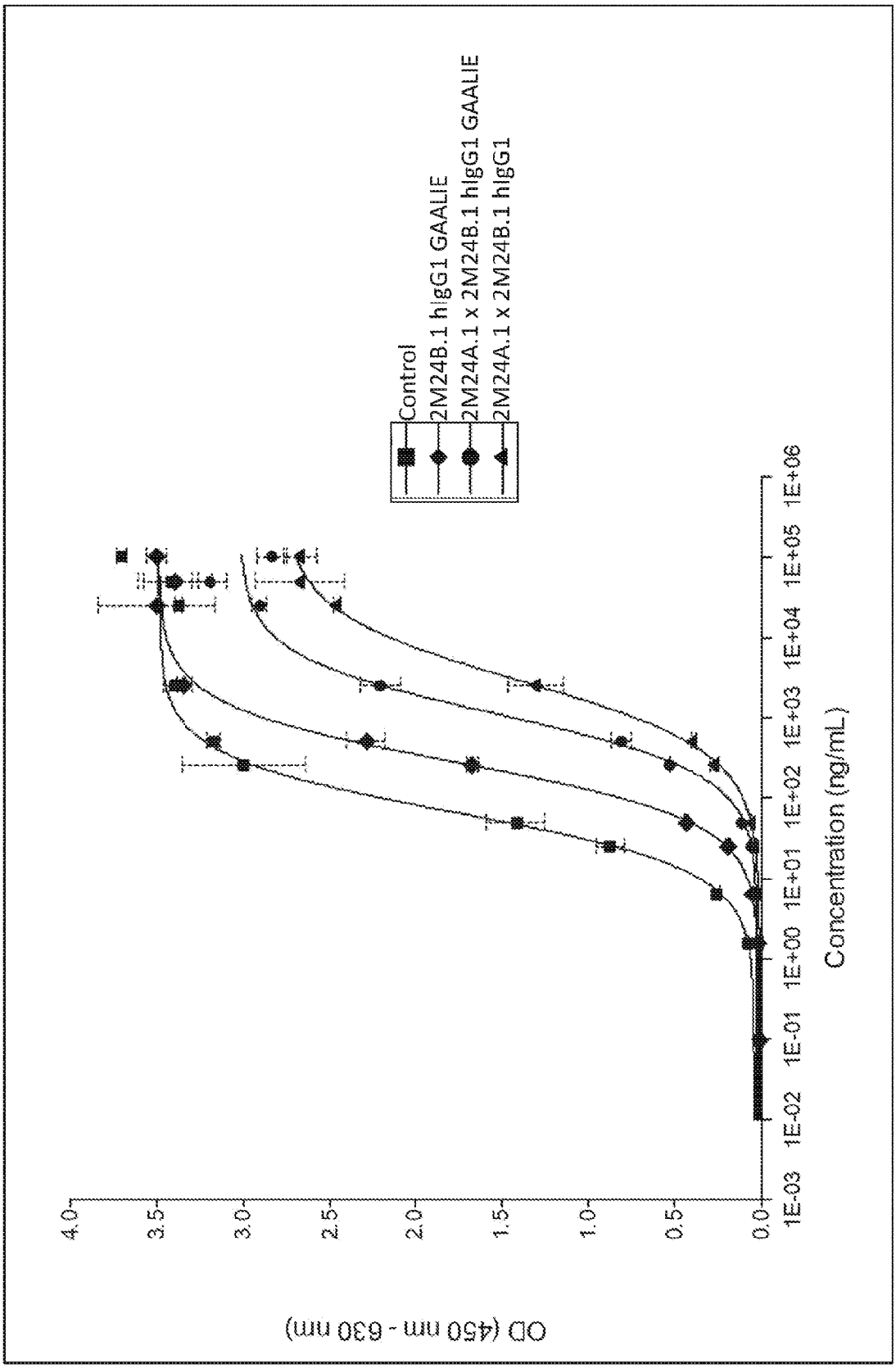

OD (450 nm - 630 nm)
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
1E-03
1E-02
1E-01
1E+00
1E+01
1E+02
1E+03
1E+04
1E+05
1E+06
Concentration (ng/mL)
Control
2M24B.1 hIgG1 GAALIE
2M24A.1 x 2M24B.1 hIgG1 GAALIE
2M24A.1 x 2M24B.1 hIgG1

FIG. 70C

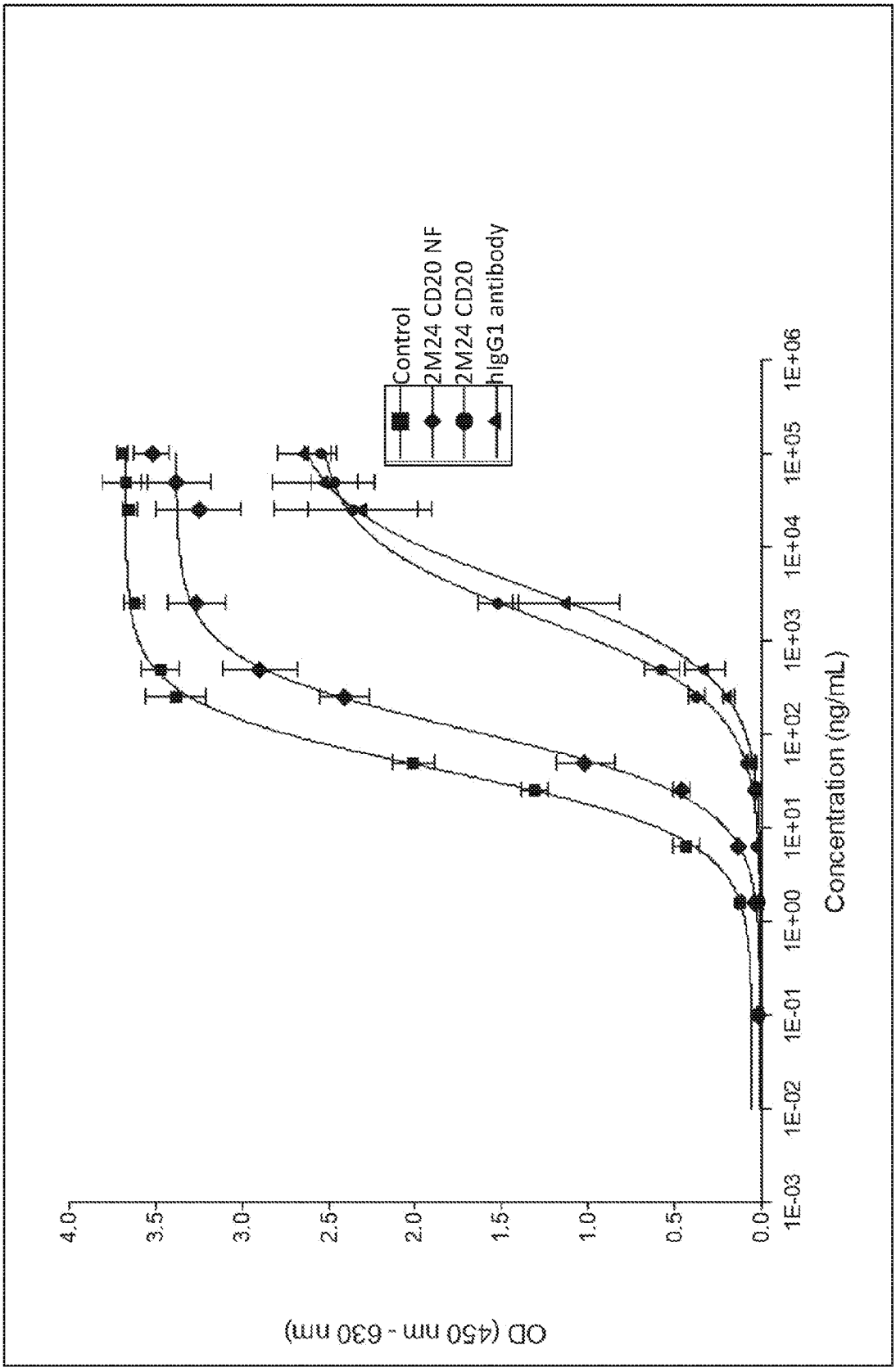

OD (450 nm - 630 nm)
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
1E-03
1E-02
1E-01
1E+00
1E+01
1E+02
1E+03
1E+04
1E+05
1E+06
Concentration (ng/mL)
Control
2M24 CD20 NF
2M24 CD20
hIgG1 antibody

FIG. 70D

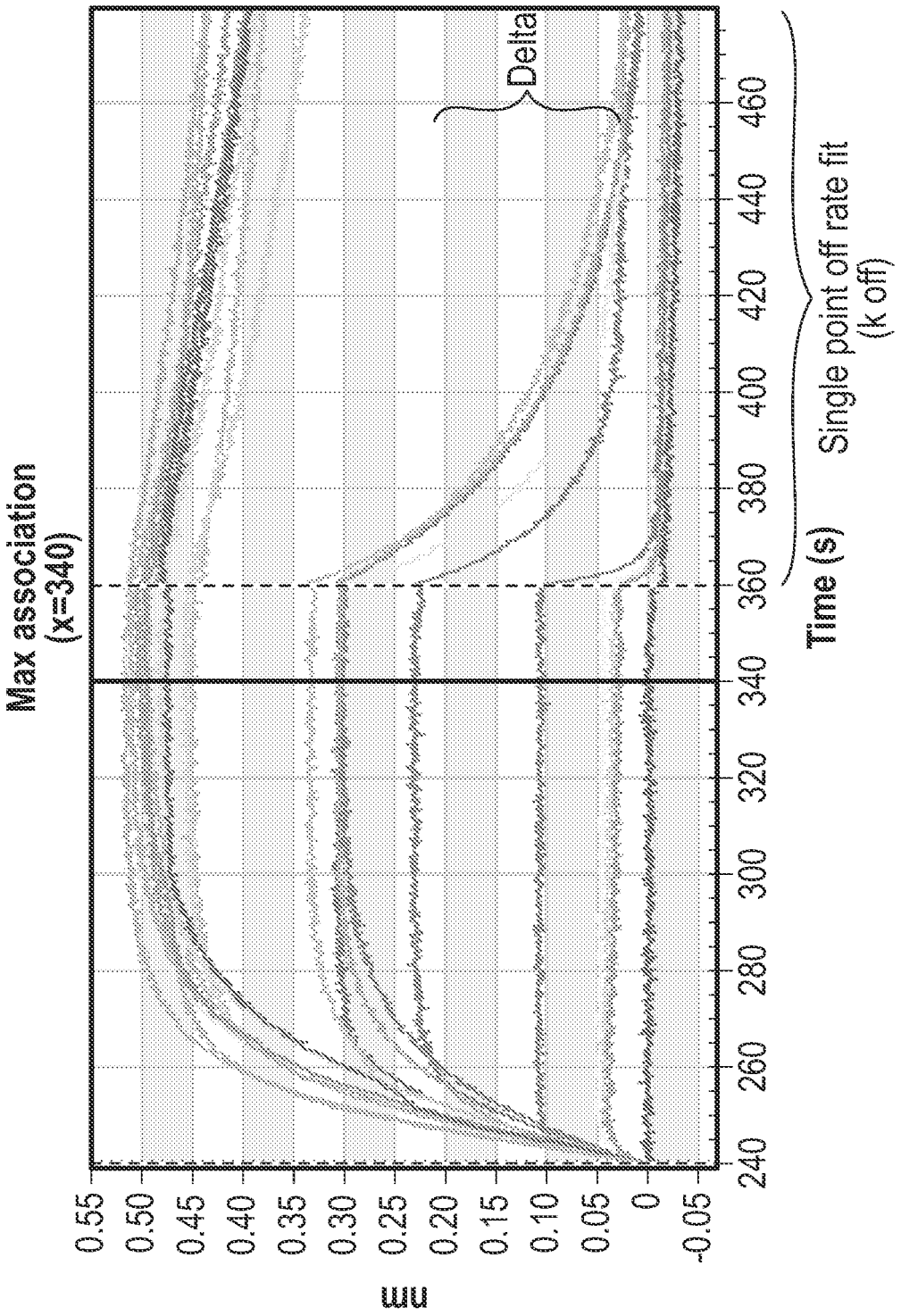

Max association
(x=340)
Delta
nm
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
-0.05
240
260
280
300
320
340
360
380
400
420
440
460
Time (s)
Single point off rate fit
(k off)

FIG. 71

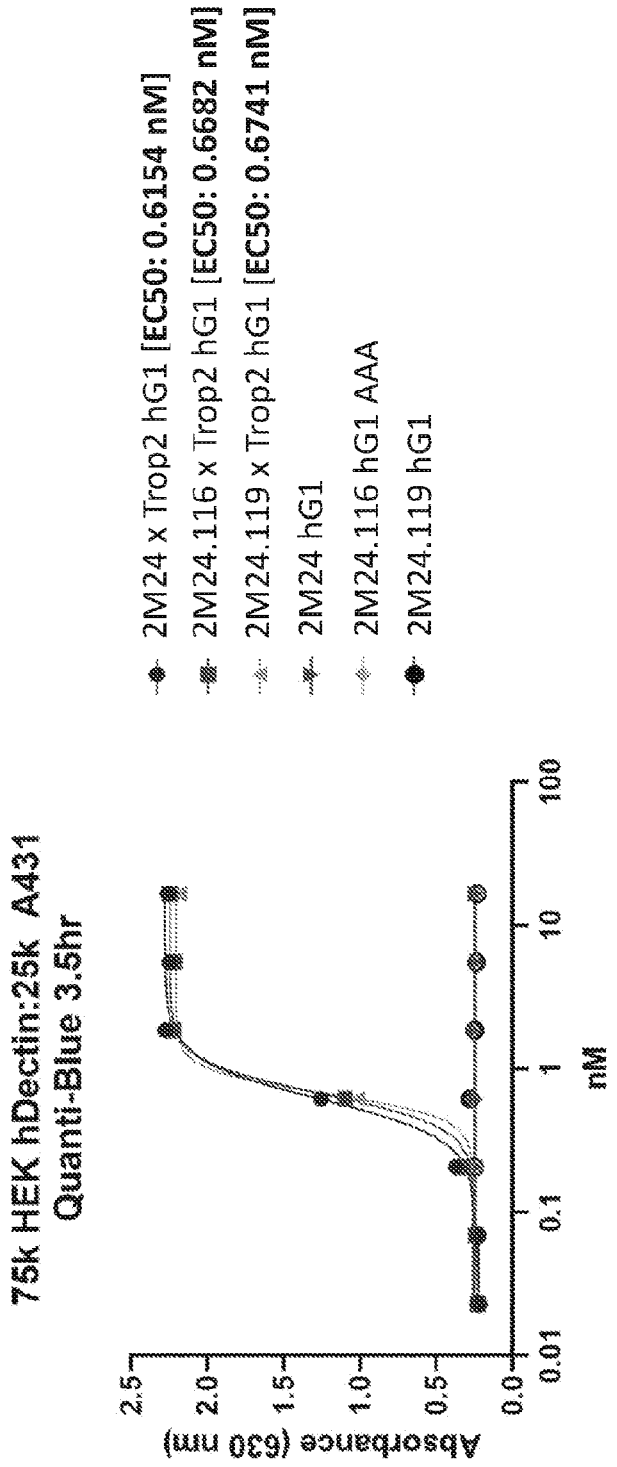

75k HEK hDectin:25k A431
Quanti-Blue 3.5hr
Absorbance (630 nm)
2.5
2.0
1.5
1.0
0.5
0.0
0.01
0.1
1
10
100
nM
2M24 x Trop2 hG1 [EC50: 0.6154 nM]
2M24.116 x Trop2 hG1 [EC50: 0.6682 nM]
2M24.119 x Trop2 hG1 [EC50: 0.6741 nM]
2M24 hG1
2M24.116 hG1 AAA
2M24.119 hG1

FIG. 72A

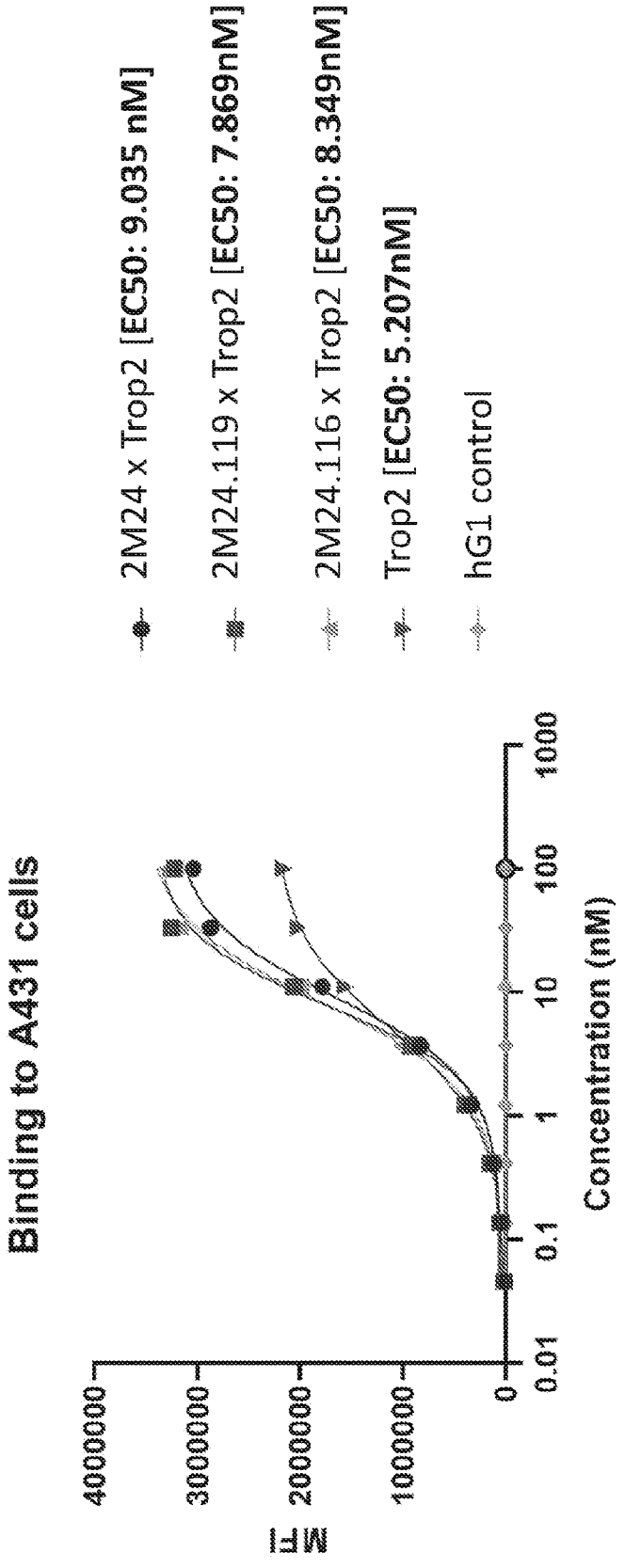

Binding to A431 cells
MFI
4000000
3000000
2000000
1000000
0
0.01
0.1
1
10
100
1000
Concentration (nM)
2M24 x Trop2 [EC50: 9.035 nM]
2M24.119 x Trop2 [EC50: 7.869nM]
2M24.116 x Trop2 [EC50: 8.349nM]
Trop2 [EC50: 5.207nM]
hG1 control

FIG. 72B

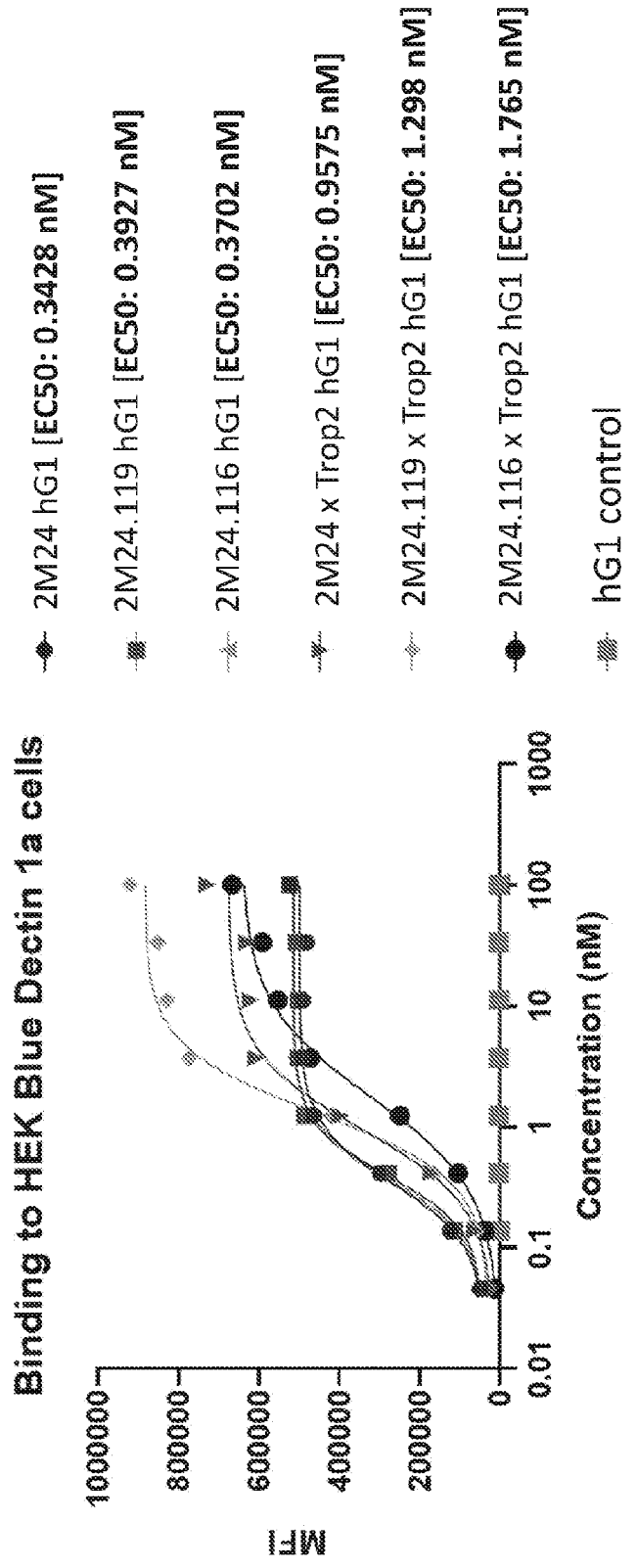

Binding to HEK Blue Dectin 1a cells
MFI
1000000
800000
600000
400000
200000
0
0.01
0.1
1
10
100
1000
Concentration (nM)
2M24 hG1 [EC50: 0.3428 nM]
2M24.119 hG1 [EC50: 0.3927 nM]
2M24.116 hG1 [EC50: 0.3702 nM]
2M24 x Trop2 hG1 [EC50: 0.9575 nM]
2M24.119 x Trop2 hG1 [EC50: 1.298 nM]
2M24.116 x Trop2 hG1 [EC50: 1.765 nM]
hG1 control

FIG. 72C

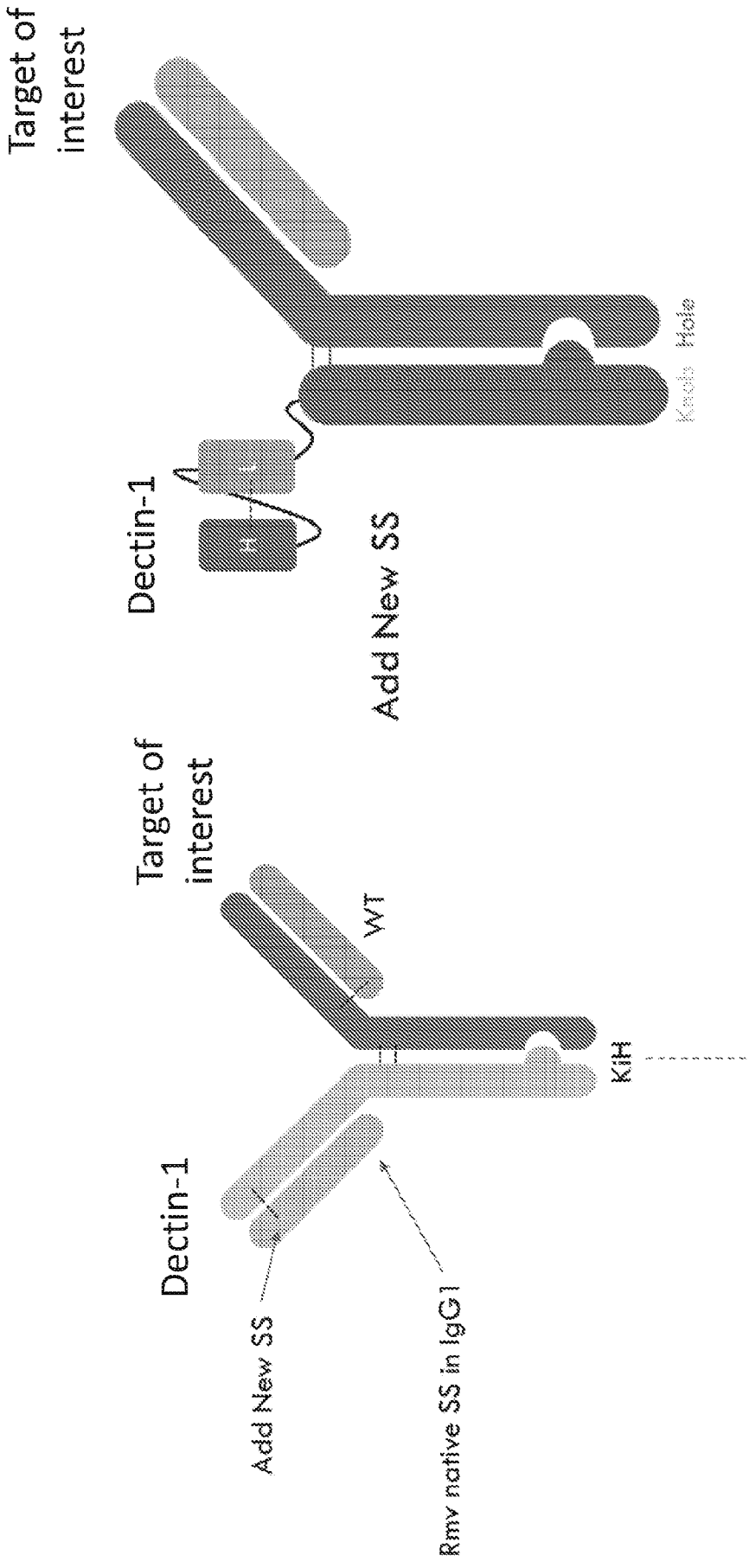

Target of interest
Dectin-1
Add New SS
Knob
Hole
Target of interest
WT
KiH
Dectin-1
Add New SS
Rmv native SS in IgG1

FIG. 73

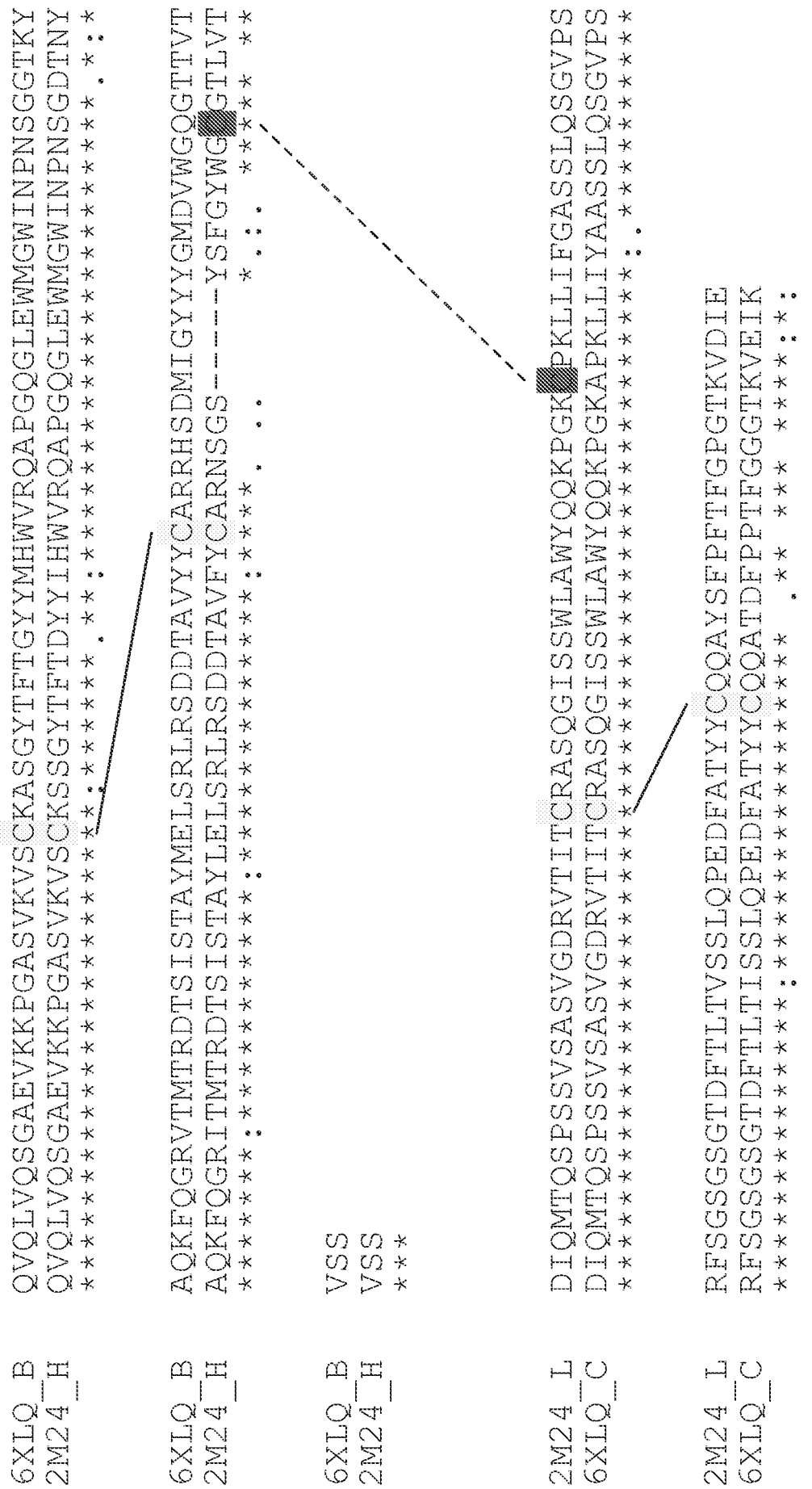

6XLQ_B QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMHWVRQAPGQGLEWMGWINPNSGGTKY
2M24_H QVQLVQSGAEVKKPGASVKVSCKSSGYTFTDYYIHWVRQAPGQGLEWMGWINPNSGDTNY
6XLQ_B AQKFQGRVTMTRDTSISTAYMELSRLRSDDTAVYYCARRHSDMIGYYYGMDVWGQGTTVT
2M24_H AQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGS----YSFGYWG GTLVT
6XLQ_B VSS
2M24_H VSS
2M24_L DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGK PKLLIFGASSLQSGVPS
6XLQ_C DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIYAASSLQSGVPS
2M24_L RFSGSGSGTDFTLTVSSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE
6XLQ_C RFSGSGSGTDFTLTISSLQPEDFATYYCQQATDFPPTFGGGTKVEIK

FIG. 74A

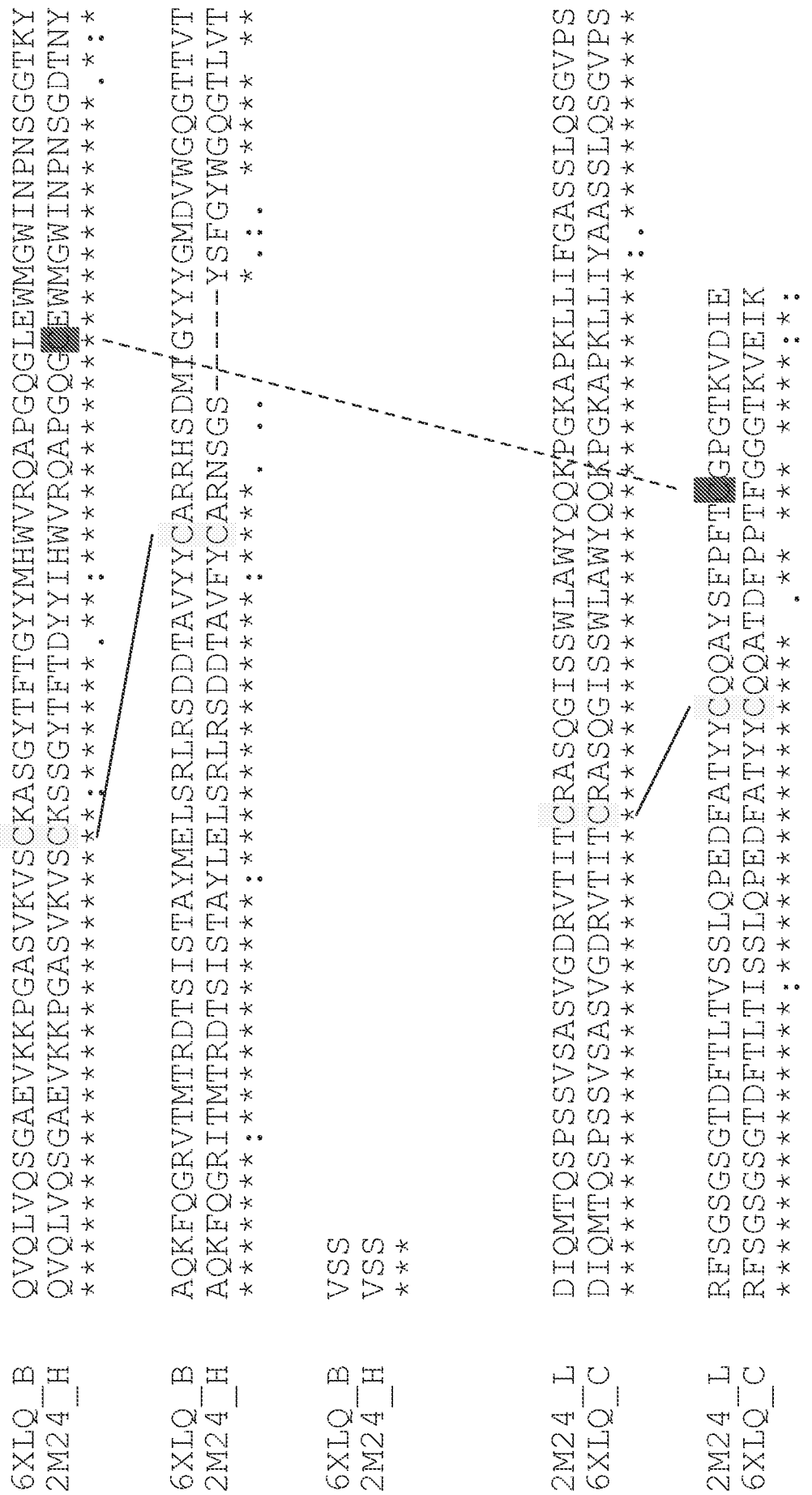

6XLQ_B QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMHWVRQAPGQGLEWMGWINPNSGGTKY
2M24_H QVQLVQSGAEVKKPGASVKVSCKSSGYTFTDYYIHWVRQAPGQGLEWMGWINPNSGDTNY
6XLQ_B AQKFQGRVTMTRDTSISTAYMELSRLRSDDTAVYYCARRHSDMIGYYYGMDVWGQGTTVT
2M24_H AQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGS----YSFGYWGQGTLVT
6XLQ_B VSS
2M24_H VSS
2M24_L DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPS
6XLQ_C DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIYAASSLQSGVPS
2M24_L RFSGSGSGTDFTLTVSSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE
6XLQ_C RFSGSGSGTDFTLTISSLQPEDFATYYCQQATDFPPTFGGGTKVEIK

FIG. 74B

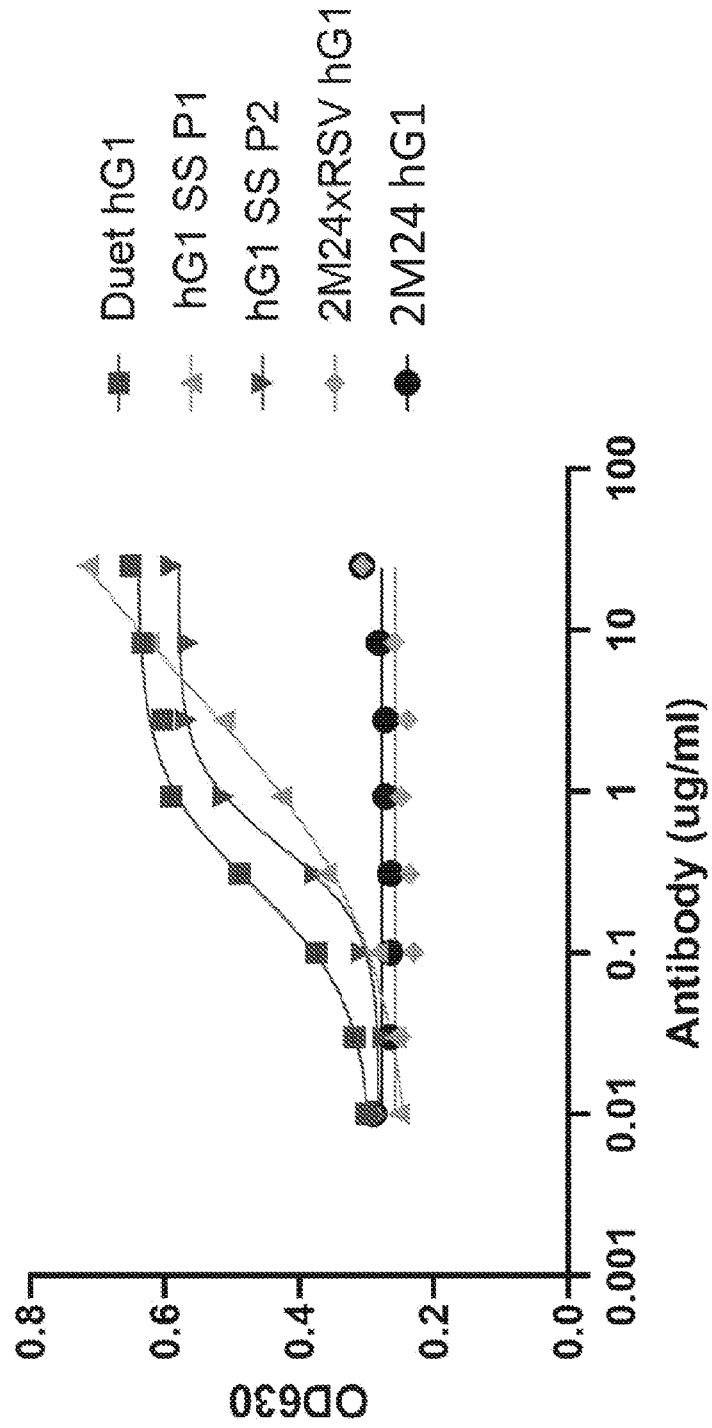

HekBlue x Raji
Duet hG1
hG1 SS P1
hG1 SS P2
2M24xRSV hG1
2M24 hG1
OD630
0.0
0.2
0.4
0.6
0.8
0.001
0.01
0.1
1
10
100
Antibody (ug/ml)

FIG. 75A

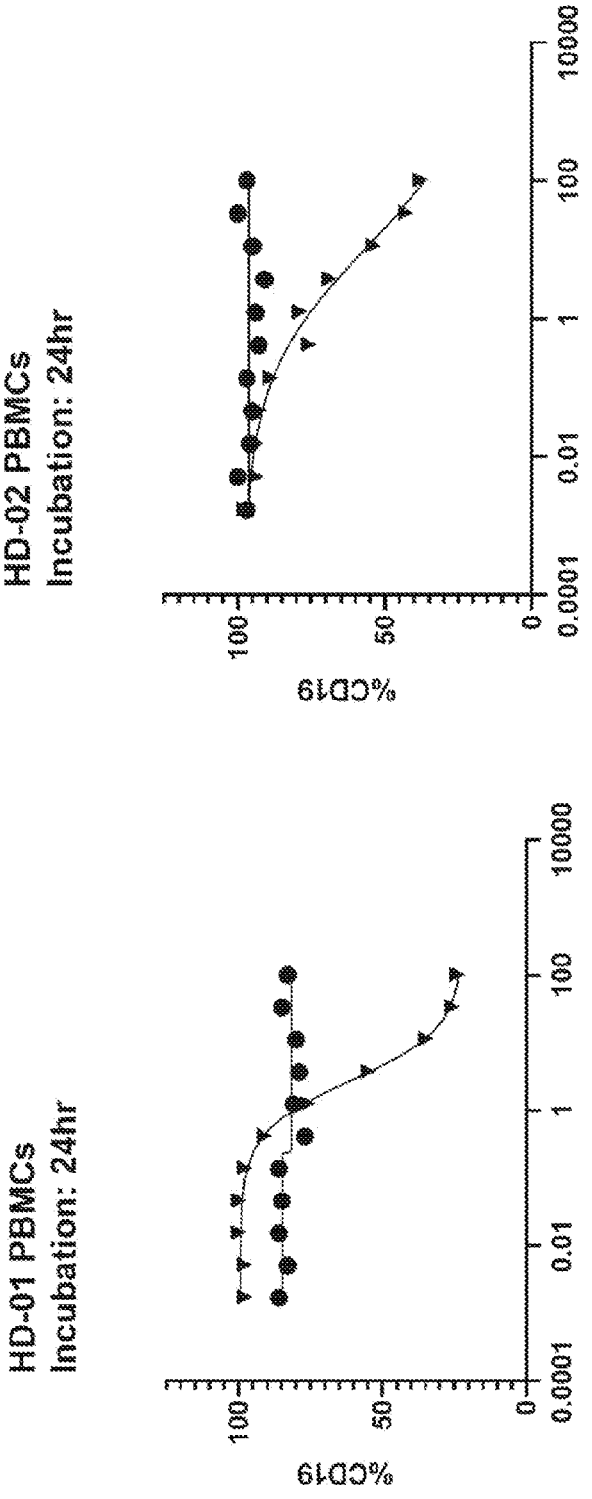
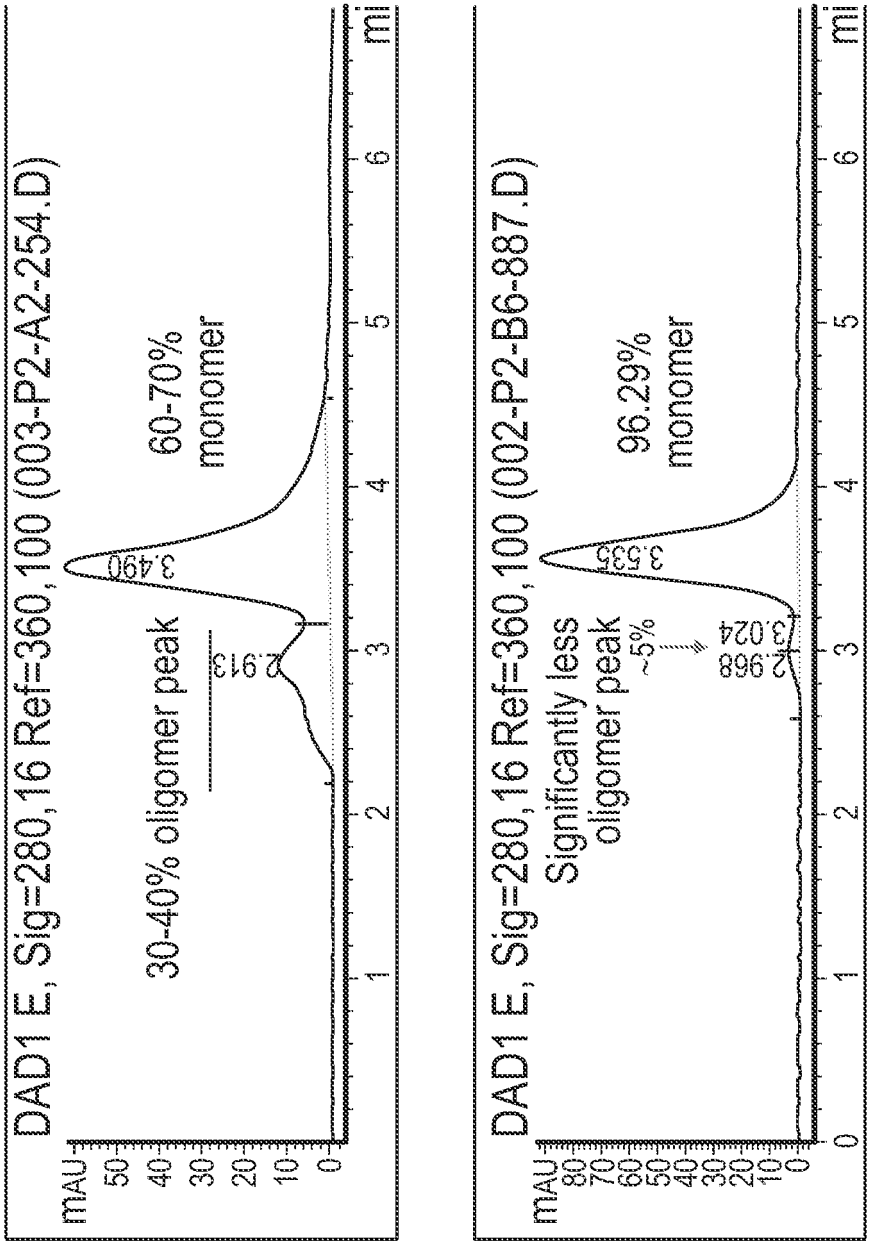

HD-02 PBMCs
Incubation: 24hr
%CD19
100
50
0
0.0001
0.01
1
100
10000
nM
2M24 P1 x CD20 hG1 SS
RSV (Iso) hIgG1
HD-01 PBMCs
Incubation: 24hr
%CD19
100
50
0
0.0001
0.01
1
100
10000
nM
2M24 P1 x CD20 hG1 SS
RSV (Iso) hIgG1

FIG. 75B


DAD1 E, Sig=280,16 Ref=360,100 (003-P2-A2-254.D)
mAU
mi
3.490
2.913
60-70% monomer
30-40% oligomer peak
DAD1 E, Sig=280,16 Ref=360,100 (002-P2-B6-887.D)
mAU
mi
3.535
3.024
2.968
96.29% monomer
Significantly less oligomer peak
~5%

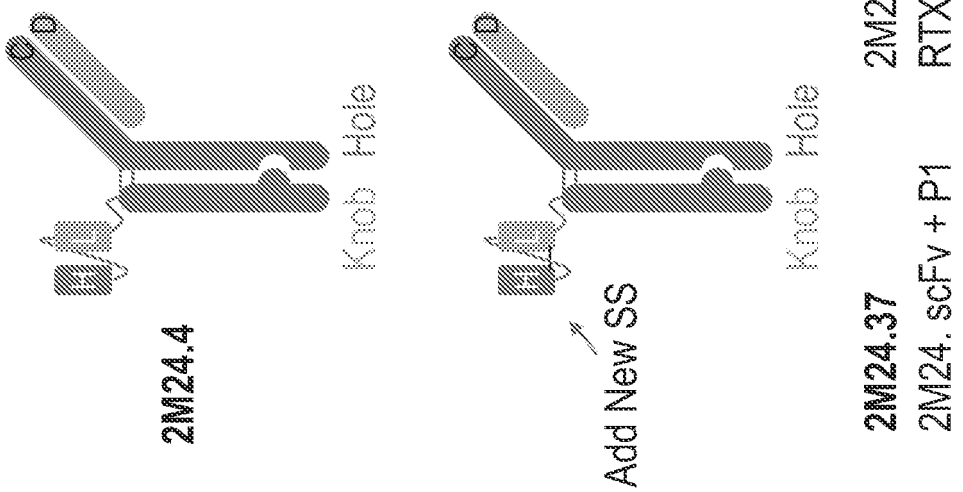

Knob
Hole
2M24.4
Add New SS
Knob
Hole
2M24.37
2M24. scFv + P1
2M24
RTX

FIG. 76A

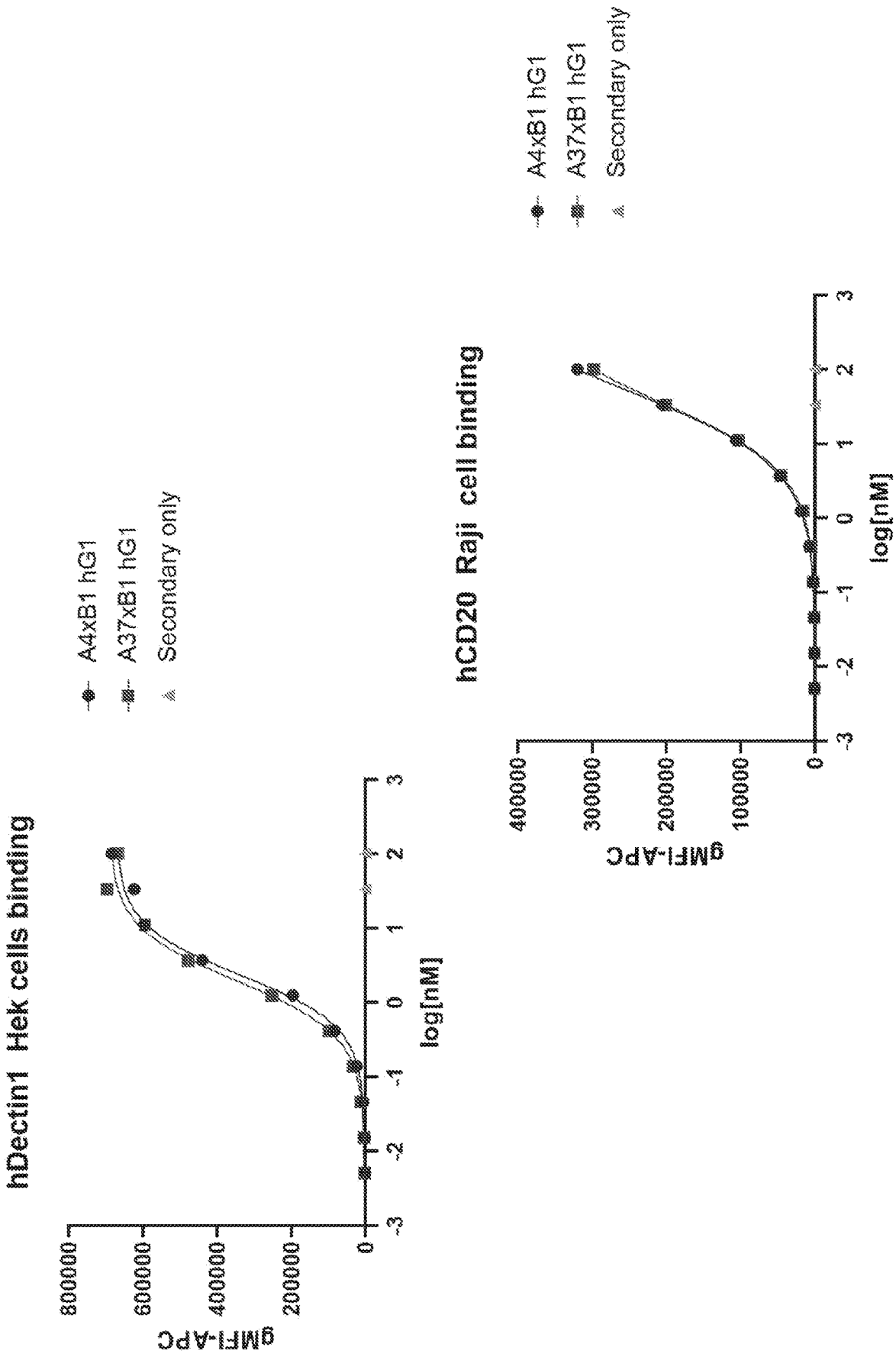

hDectin1 Hek cells binding
A4xB1 hG1
A37xB1 hG1
Secondary only
gMFI-APC
800000
600000
400000
200000
0
-3
-2
-1
0
1
2
3
log[nM]
hCD20 Raji cell binding
A4xB1 hG1
A37xB1 hG1
Secondary only
gMFI-APC
400000
300000
200000
100000
0
-3
-2
-1
0
1
2
3
log[nM]

FIG. 76B

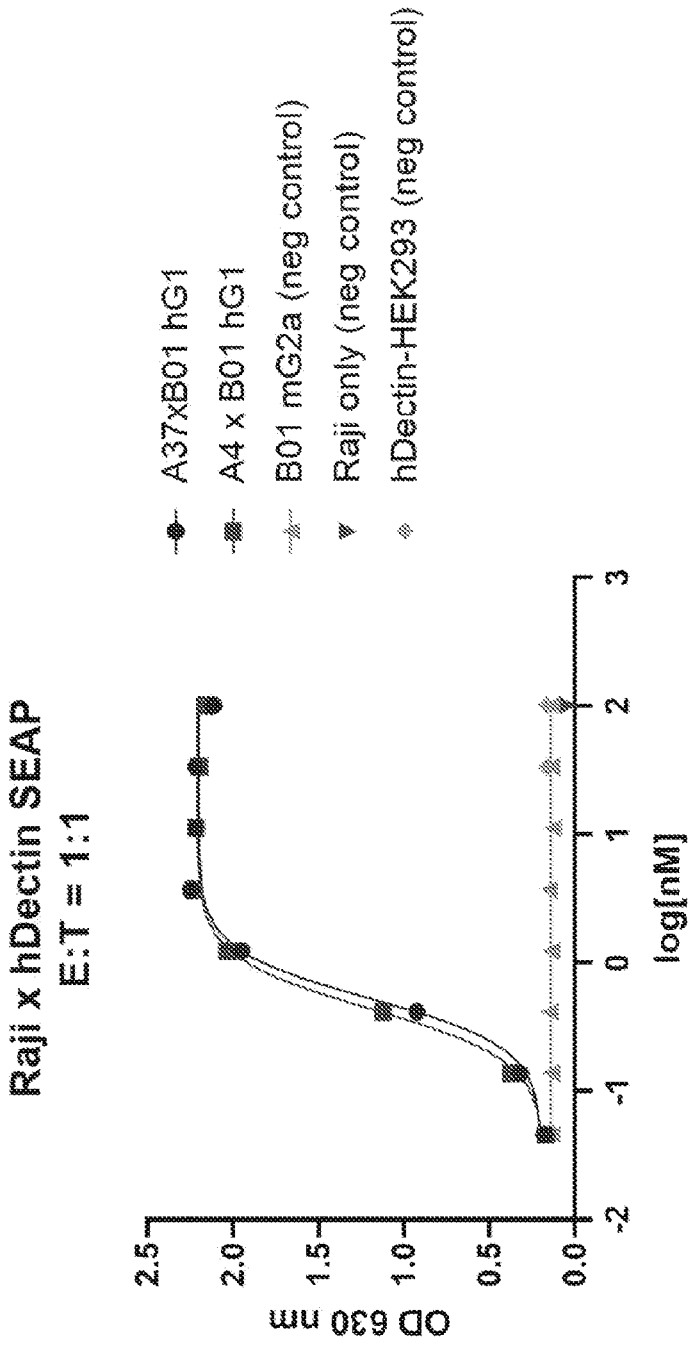

Raji x hDectin SEAP
E:T = 1:1
A37xB01 hG1
A4 x B01 hG1
B01 mG2a (neg control)
Raji only (neg control)
hDectin-HEK293 (neg control)
OD 630 nm
2.5
2.0
1.5
1.0
0.5
0.0
-2
-1
0
1
2
3
log[nM]

FIG. 76C

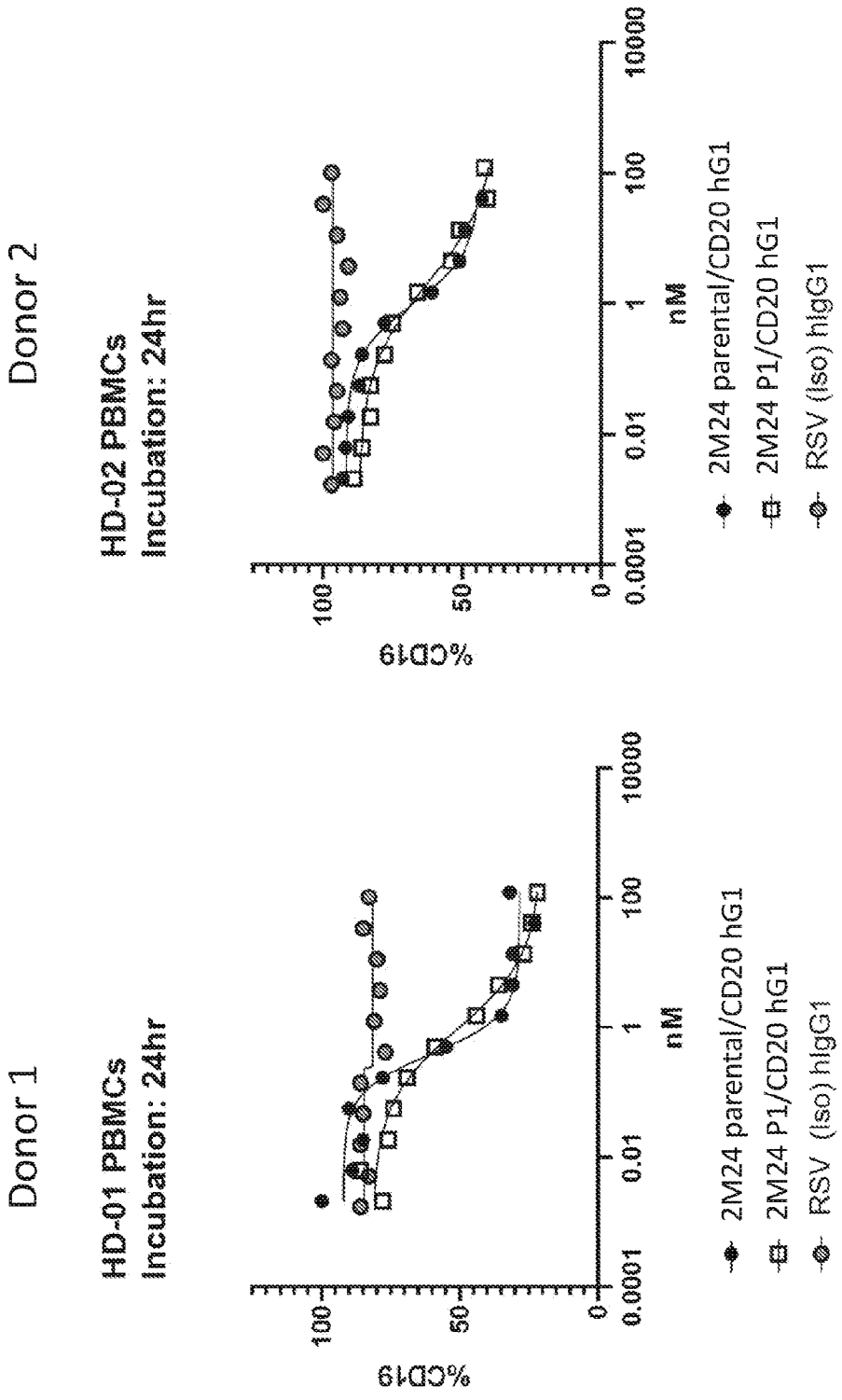

Donor 1
HD-01 PBMCs
Incubation: 24hr
%CD19
100
50
0
0.0001
0.01
1
100
10000
nM
2M24 parental/CD20 hG1
2M24 P1/CD20 hG1
RSV (Iso) hIgG1
Donor 2
HD-02 PBMCs
Incubation: 24hr
%CD19
100
50
0
0.0001
0.01
1
100
10000
nM
2M24 parental/CD20 hG1
2M24 P1/CD20 hG1
RSV (Iso) hIgG1

FIG. 76D

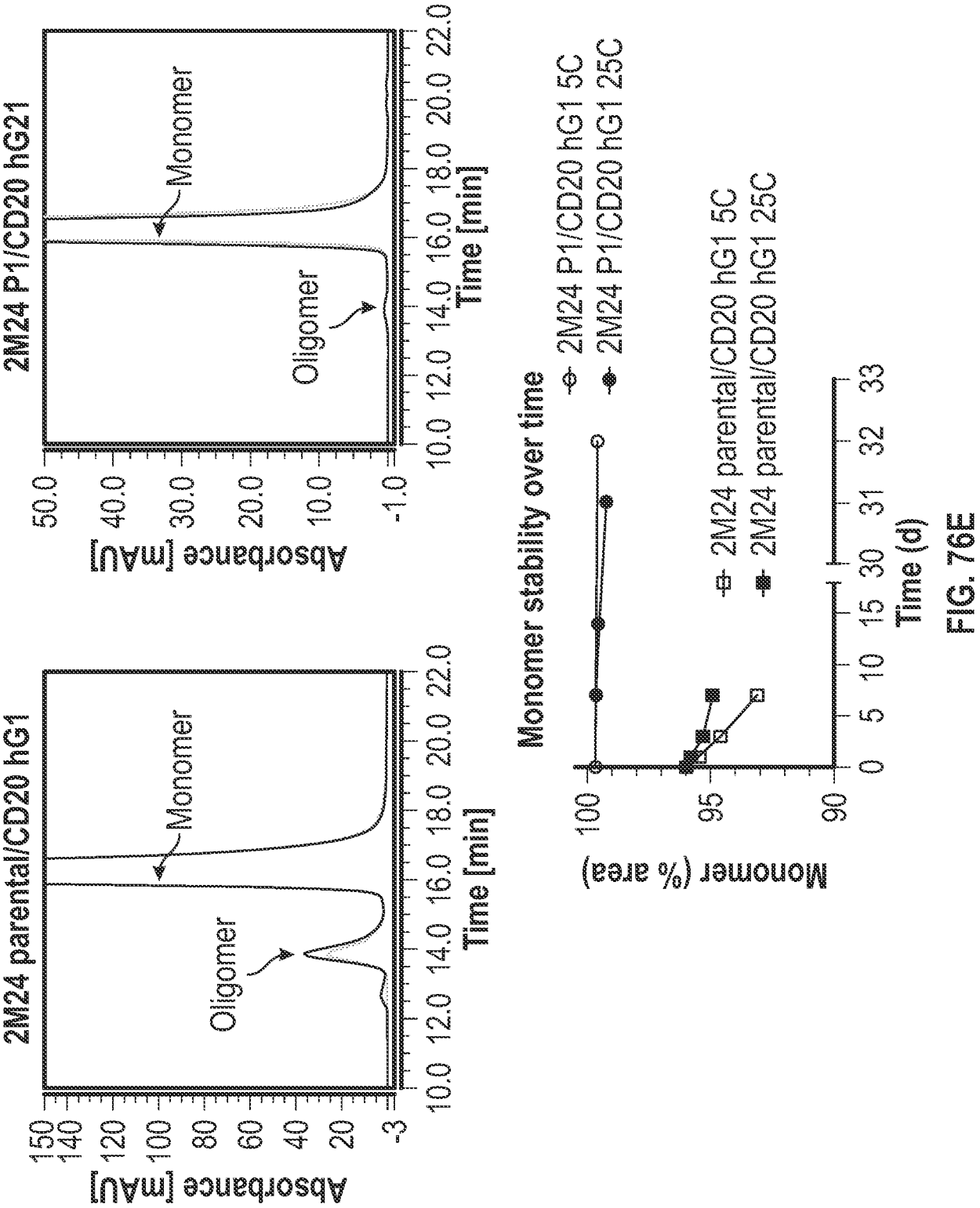

2M24 parental/CD20 hG1
Monomer
Oligomer
Absorbance [mAU]
Time [min]
2M24 P1/CD20 hG21
Monomer
Oligomer
Absorbance [mAU]
Time [min]
Monomer stability over time
2M24 P1/CD20 hG1 5C
2M24 P1/CD20 hG1 25C
2M24 parental/CD20 hG1 5C
2M24 parental/CD20 hG1 25C
Monomer (% area)
Time (d)

FIG. 76E

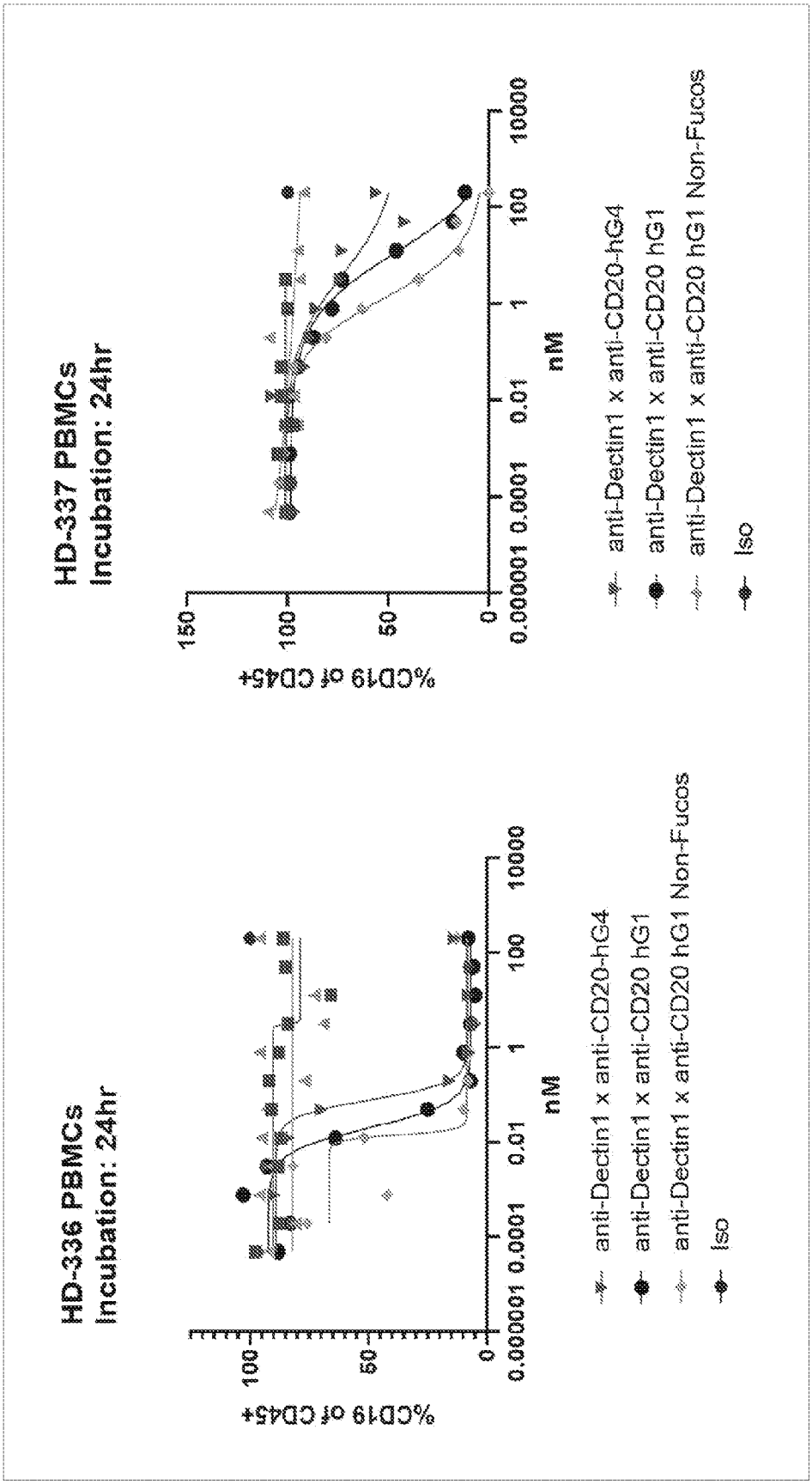

HD-336 PBMCs
Incubation: 24hr
%CD19 of CD45+
100
50
0
0.000001 0.0001 0.01 1 100 10000
nM
HD-337 PBMCs
Incubation: 24hr
%CD19 of CD45+
150
100
50
0
0.000001 0.0001 0.01 1 100 10000
nM
anti-Dectin1 x anti-CD20-hG4
anti-Dectin1 x anti-CD20 hG1
anti-Dectin1 x anti-CD20 hG1 Non-Fucos
Iso

FIG. 77

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